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PROBLEMS OF SPACE BIOLOGY

VOLUME 5

Dynamics of the Cerebral Blood Volume Under Normal Conditions and Gravitational Stresses

by Yu. Ye. Moskalenko

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By Yu. Ye. Moskalenko

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Yu. Ye. Moskalenko

FOREWORD

The rapid development of space science and the progress recently made in /5
this field have stimulated a great deal of interest in it on the part of a variety of specialists. The prospects for manned spaceflight require the solution of an increasing number of new and difficult problems. One of these is blood circulation under conditions of an altered gravitational field.

It is common knowledge that spaceflight entails exposure to accelerations and weightlessness, factors that living organisms normally do not encounter on earth. The results of many biological experiments as well as studies made by cosmonauts during flights have produced extensive data on reactions of the cardiovascular system to these extraordinary conditions. The general picture of the changes proved to be fairly complex chiefly because of the immense role played by the circulatory system in maintaining the basic physiological constants and working apparatus of the body. Yet until recently biologists had comparatively meager information on the state of the peripheral circulation, especially the cerebral, during exposure to spaceflight factors. This situation made it very difficult to interpret the experimental material, elucidate the mechanisms of the physiological action of the gravitation factor, and devise the necessary preventive measures.

The results of investigations on the dynamics of the cerebral blood circulation under both normal conditions and gravitational stresses that were carried out by Yu. Ye. Moskalenko and his associates in the Sechenov Institute of Evolutionary Physiology and Biochemistry are very relevant to a solution of the problem. This monograph contains the only summary of the many years' work done by the author in this timely field.

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INTRODUCTION

Intracranial hemodynamics occupies a special position among the various branches of cardiovascular physiology. From the standpoint of timeliness, data /6
on intracranial hemodynamics are essential not only in the study of cerebral circulation but also to solve some neurophysiological problems. As long ago as 1895 Zhukov noted in the Bol'nichnaya gazeta im. Botkina (Botkin Hospital Gazette) (p. 1092): "No single function, regardless of the organ, is as closely related to the state of blood circulation as the activity of the nerve centers." The significance of this view has grown, especially in our times when studies on various aspects of cerebral activity have come to be central in modern physiology. Therefore, matters pertaining to the physiology of the intracranial blood circulation can rightly be considered neurophysiological matters.

The intracranial blood circulation can also be considered a clinical problem. Everyone is aware of the seriousness of vascular disorders of the brain, which rank third in causes of death after heart disease and cancer (Simonson and MacGavak, 1964). Progress in treating these disorders is largely dependent on the level of knowledge of the physiology of cerebral circulation.

It is no accident, therefore, that the subject of cerebral blood circulation has for many years been in the forefront of attention of specialists in many fields. The number of publications has increased substantially in recent years. For example, according to the annotated bibiliography of Soviet literature on the craniocerebral circulation,* 32 works were published in the 19th century, 60 from 1900 to 1950, but more than 250 from 1950 to 1964. Some idea of the /7
total number of publications now available in the world literature can be gained from the fact that an annotated bibliography on the functional anatomy and physiology of the cerebral circulation issued in 1952 contained about 4000 titles.

Study of the intracranial circulation presents much more difficult technical problems than does that of other parts of the cardiovascular system. The reason is that the organs of the central nervous system have a bony case impairment of whose integrity in the course of investigations results in distortion of the observed phenomena. The consequence is that many publications on the physiology of the intracranial circulation contain some debatable, unexplained views based on contradictory and sometimes unreliable facts.

It follows from the above that the physiology of the intracranial circulation is now a multifaceted scientific field dealing with a number of problems each of which requires deep and planned study using special methods. This conclusion is supported by the history of the study of the subject in recent years, which shows that unlike the works published prior to the 1950s, the most thorough studies now undertaken deal with comparatively narrow problems. For example, the morphology and physiology of the cerebral circulation has found detailed expression in the monographs of Klosovskiy (1951) and Klosovskiy and

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A. I. Naumenko and M. N. Suprun, 1964. Soviet Bibliography on the Cerebral Circulation. Library of the First Leningrad Medical Institute.

Kosmarskaya (1961). Studies on measurement of the rate of blood flow through the brain and the linear velocity of the cerebrospinal fluid (CSF) are rigorously analyzed in the monograph of Vasilevskiy and Naumenko (1959). Mchedlishvili (1966) summarized thorough carefully planned studies on regulation of the blood flow in the regional (internal carotid and vertebral) and pial arteries of the brain. The identification and concretization of the main problems in the physiology of intracranial blood circulation is also suggested by the names of symposia held during the past few years: Physiological Mechanisms of Regulation of the Cerebral Circulation (Tiflis, 1963) and Cerebral Ischemia (Florida, 1962).

This monograph too deals with a fairly narrow problem - the mechanisms of compensation of changes in the blood volume of the cranial cavity under both normal conditions and gravitational stresses, with attention focused mainly on the biophysical aspects. It aims at elucidation of the general principles governing the dynamics of the cerebral blood volume under normal conditions and during the redistribution of blood caused by gravitational forces, but does not /8 go into the physiological mechanisms regulating the cerebral blood volume or cerebral blood flow. Use was made of material obtained in acute and chronic experiments on animals and during observations on human beings aided by intracranial electroplethysmography and other biophysical methods.

The mechanisms of intracranial blood circulation constitute one of the major problems in the physiology of the cerebral blood volume. The processes that take place in the cerebrovascular system involve complex physical and physiological phenomena. Ultimately, however, any changes in the cerebral circulation, whether physiological or physical in nature, are reflected in changes in the blood volume of the individual vascular basins of the cranial cavity.

Local and general changes in the cerebral blood volume result from a great variety of causes. Normally, periodic changes arise from the activity of the heart and respiratory movements. There are also third-order waves (Meyer waves). Nonperiodic changes arise both from active regulatory processes in the cerebral circulatory system and from the effects of physical factors. Among the commonest of the natural influences are minor longitudinal gravitational stresses caused by gravity. These stresses bring about a redistribution of the blood during vertical changes in body position.

Under natural conditions all living organisms experience longitudinal accelerations with maximum limits of ±1G which corresponds to a strictly vertical position of the body - head up or head down. The values of the stresses experienced under natural conditions vary with the way of life and mobility of the individual organisms. Some animals, moreover, experience brief accelerations of around 2 g when starting to run, and shock overloads of up to 10 to 15 g arise during a jump from a height of about 1 m.

The value of a longitudinal gravitational stress acting on the intracranial /9 circulation with the body inclined (as in fig. 1) is:

$$g' = g_0 \sin \theta,$$

where g_0 is the acceleration of terrestrial gravity, θ is the angle of inclination

of the longitudinal axis of the body to the horizontal plane.

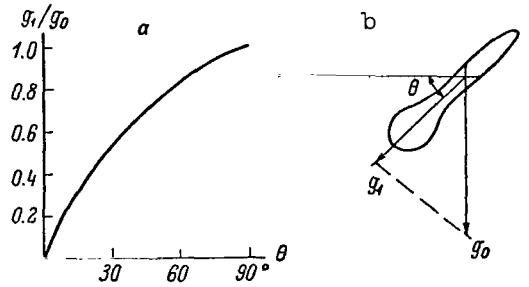

Figure 1. Relationship of the value of the longitudinal gravitational stress to the value of the angle of inclination of the body to the horizontal plane (a) and diagram of the forces acting on an animal with the body in inclined position (b).

θ - angle of inclination of the body to the horizon; g_0 - force of terrestrial gravity; g_1 - its component directed along the body.

It is common knowledge that the main arteries and veins responsible for supplying the brain with blood parallel the longitudinal axis of the body. Hence, the influence of longitudinal accelerations on the cerebral circulation vary with their direction. With acceleration acting in a pelvis-head direction or with negative acceleration,* the force of gravity will promote the flow of arterial blood to the head and hamper the outflow of venous blood, increasing both arterial and venous pressure slightly. Consequently, the cranial blood volume must increase. With a stress acting in a head-pelvis direction or with a positive acceleration, both arterial and venous pressure will fall, causing the cerebral blood volume to decrease. Thus, longitudinal accelerations acting on living organisms under natural conditions alter the blood volume of the cranial cavity.

Since the development of high-speed aviation in the 1940s man has had to contend with artifical gravitational stresses of 2 to 3 g. This called attention for the first time to the great pratical value that might accrue from studying the dynamics of the cerebral blood volume in relation to the redistribution of blood caused by gravitational forces.

The importance of the subject has grown considerably in recent years owing to the progress made in building rockets. This has led to the creation of rockets capable of orbiting a spaceship with a man on board. It is common knowledge that intense accelerations are involved. The results of laboratory experiments and /10

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We are using here and in what follows Hardy's terminology (1964) for the direction of gravitational factors.

the data obtained during the flights of humans and animals (Henry et al., 1951; Lindberg et al., 1960; Hershgold and Steiner, 1960; Rossanigo and Meineri, 1961; Kiselev, 1962; Duvoisin et al., 1962; Kas'yan, 1963; Gazenko et al., 1964; Yazdovskiy, 1964; Howard and Glaister, 1964; Lamb, 1964; Lamb et al., 1964; others) showed that accelerations produce marked abnormalities in the behavior of the cardiovascular system due to the redistribution of blood. According to a good deal of indirect evidence, the blood supply of the brain is thereby impaired and this may, in turn, result in disturbances of the central nervous system. This means that at the present stage in the conquest of space the gravitational factor is a serious threat, the elimination of which requires the use of special measures such as planned training, definite position of the cosmonaut's body in relation to the direction of the acceleration, etc.

It is reasonable to assume from the foregoing that in forthcoming interplanetary flights, when man will inevitably have to cope with even greater accelerations, in magnitude and duration, flight routines will be determined not by the technical capabilities of the spacecraft or by power considerations, but by the physiological capabilities of the cosmonaut who will have to retain his fitness during the flight.

Therefore, the matters pertaining to the study of the dynamics of the cerebral blood volume during gravitational stresses naturally constitute one of the chapters in the new scientific discipline of space biology. The dynamics of the cerebral blood volume during gravitational stresses is of great interest as the theoretical basis of one of the possible ways of increasing the resistance of man and animals to altered gravitational fields.

Study of the dynamics of the cerebral blood volume during gravitational stresses has to be based on information concerning its behavior under normal conditions. However, we do not know much about it. One of the main and unique features of the intracranial blood circulation is that changes therein take place in a closed space - the brain case. It was to be expected, therefore, /11 that in the course of evolution special mechanisms would be created to compensate changes in the cerebral blood volume.

The compensation of changes in the blood volume of the closed cranial cavity has been the subject of numerous fundamental studies (Ecker, 1844; Richet, 1846; Quincke, 1872; Salathe, 1876; Blumenau, 1889; Nagel', 1889; Geigel, 1905; Becher, 1922; Ewig and Lullies, 1924; Sepp, 1927, Hurthle, 1927; O'Connell, 1943; Ryder, 1952; Ryder and Espey, 1952; Ryder et al., 1952; Kedrov and Naumenko, 1954 ; Fridman, 1957; Vasilevskiy and Naumenko, 1959). These studies suggest that changes in the cerebral blood volume can theoretically be compensated in two ways: (1) by change in the correlation of volumes of arterial and venous blood in the cranial cavity, and (2) by movement of some CSF between the cerebral and spinal cavities, i.e., by change in the correlation of the volumes of the blood and CSF in the cranial cavity.

However, the difficulty of studying the intracranial circulation and the imperfect methods available have led to major conflicting interpretations of the basic phenomena. For example, the question of pulsation in the closed cranial cavity is still moot. Those who believe that pulsation is present include Richet (1846), Pirogov (1864), Mosso (1881), Nagel' (1889), Blumenau

(1889), Grashey, 1892, Verigo (1905), Reznikova and Davidenkova (1911), Sepp (1928), Alov (1949), Kedrov and Naumenko (1954), Moskalenko (1961). Opponents of this view include Donders (1851), Leyden, 1886), Navalikhin (1874), Riser, 1936), Forbes and Cobb (1938), Klosovskiy (1951), Sigward, 1954), Feruglio (1954), and Brain, 1957). Nor is there any consensus on the direction in which the CSF moves in the submeningeal spaces of the brain and spinal cord. Some investigators (Hill, 1896; Jacobi, 1923; Spirov, 1927; Gardner, 1944; Avtandilov, 1956; Vasilevskiy and Naumenko, 1959; others) think that it moves in a caudal direction, but an equal number (Jacobi, 1900; Woolsey, 1915; Strecker, 1922; Ivanov, 1935; Shamburov, 1954; others) hold the opposite view. Still others (Falkenheim and Naunyn, 1887; Walter, 1910; Sachs et al., 1930; others) are of the opinion that the CSF does not move at all between the cranial and spinal cavities.

These differences of opinion throw doubt on the existence of compensatory movements of the CSF between the cranial and spinal cavities following changes in the volume of cranial blood, i.e., on one of the principal means of compensating changes in the blood volume of the closed cranial cavity. /12

Equally debatable are the results of some biophysical studies that sought to show by theoretical calculations that there are mechanisms existing to compensate changes in the cerebral blood volume. For example, Geigel (1905) was sharply criticized by Sepp (1928) who was himself later criticized by Klosovskiy (1951). These examples clearly show that the difficulties in studying these mechanisms are still far from a solution.

The foregoing led us to take up the subject. In studying the mechanisms governing the compensation of changes in the blood volume under normal conditions and during gravitational stresses we used the method of electroplethysmography, which makes it possible to judge the dynamics of the cerebral blood volume directly. It is thus the best method to use in solving the problem.

On the basis of the data that we obtained with the help of electroplethysmography and other methods and from a critical analysis of the experimental material of other investigators, we shall describe in this monograph the basic mechanisms responsible for compensating changes in the blood volume of the closed cranial cavity. In addition to analyzing the nature of the activity of these mechanisms during compensation of periodic fluctuations in the blood volume resulting from cardiac activity, respiratory movements, third-order waves, and vascular reactions of the brain under normal conditions, including longitudinal gravitational accelerations of up to +1 g, we shall also consider some aspects of the active and passive compensation of changes during gravitational stresses of more than 1 g, such as living organisms encounter in the course of spaceflight. In order to define concretely the matters under discussion we shall examine the dynamics of the cerebral blood volume as a partly isolated system without going into the reasons for the inflow or outflow of blood from the brain as a result of gravitational stresses.

CHAPTER 1. ELECTROPLETHYSMOGRAPHIC METHOD OF INVESTIGATING THE INTRACRANIAL CIRCULATORY SYSTEM

The investigation of the intracranial circulatory system is a complex, /13
methodological problem. A large number of methodological approaches to the investigation of this system have been proposed over several decades. However, most of the known methods of investigation, while making it possible to observe the individual aspects of the cerebrovascular system activity, do not make it possible to represent the operation of the system as a whole and also are limited from the standpoint of sensitivity and response of recording. The application of some of the methods is associated with substantial injury to the experimental animals. A great deal of complexity associated with the investigation of intracranial circulation involves the estimation of recording errors introduced by a particular method. This is particularly significant when indirect methods, which have become quite common in recent years, are used in the investigation. All these factors are responsible for a certain amount of contradiction and occasional unreliability of collected factual material, which serves as a basis for certain propositions concerning the physiology of intracranial circulation.

Thus, in carrying out specific investigations of cerebral circulation it is quite significant to select a method which is particularly suited to the formulated problem with respect to the possibility of recording the necessary quantities, sensitivity, frequency response, and error magnitude.

For these reasons the present chapter is devoted to methodological problems. The purpose of the chapter is: a) to acquaint the reader with modern methodological approaches to the study of intracranial circulation; to illustrate the biophysical basis and possibilities of the method of intracranial electroplethysmography; b) to show thatits application is highly expedient in comparison with that of other methods for the investigation of mechanisms of the compensation of blood volume changes in the cranial cavity under normal conditions /14
and during increased gravity; c) finally, to acquaint the reader with other methods, recording equipment, and experimental techniques used by us in the investigation of intracranial circulation.

Section 1. Basic Methods of Investigating the Intracranial Circulatory System and Criteria for Their Evaluation

Several criteria must be taken into account when we evaluate the applicability of a method to the investigation of certain aspects of intracranial circulation.

First of all, such criteria include the informativeness of the method, determined by the processes which can be recorded by means of a given method. Frequently it is easy to establish the informativeness of the method but sometimes, particularly when indirect methods are used, the association of recorded quantities with processes in a cerebral vascular system is not obvious. This

makes it difficult to establish the informativeness of a given method, thus making its application of doubtful expedience. The informativeness of a method is also determined by the nature of the recorded parameters, specifically by whether a quantitative analysis of the resulting data is possible.

A comparison of the informativeness of a method with the problems to be investigated makes it possible to estimate the degree of information sufficiency when such information is obtained by means of a specific method. In some problems of investigation, a given method may provide a sufficient volume of information while in other problems the data obtained by means of a specific method must be supplemented with data obtained through other methods.

The reliability of information obtained by a particular method of investigation is highly significant and is determined by the nature and magnitude of errors inherent in a given method. The errors in the methods for investigating intracranial circulation may be divided into three groups.

1. Errors produced by the experimental conditions acting on the process under investigation (injury to the experimental animal caused by the installation of various sensors, the action of physical and chemical agents used in the investigation, etc.). These errors can be reduced to a minimum value with the aid of special investigations directed toward the search for conditions under which the action of these factors is reduced to the threshold value.

2. Errors produced by the action of processes on the recorded indicators when such processes are not associated with changes in the circulation in the region under investigation. This form of error inherent in the indirect methods of investigation is most difficult to take into account. The only radical approach for taking them into account and minimizing them is a strict physical and physiological analysis of the theoretical basis for a method. /15

3. Errors occurring during the recording of various indicators and the processing of measurement results or of the grapnic recording, instrument errors. These errors can be taken into account by means of special statistical methods for processing the results of the experiment.

The localization of the investigated region is very important when studying the individual vascular reservoirs associated with the intracranial circulatory system. From this standpoint, the importance of a method is determined by the possibility of determining most accurately the boundaries associated with the investigated region of the cerebral vascular system. In evaluating the possibility of studying local changes in circulation, it should be noted that some of the known methods of investigation make it possible to localize the investigated region geometrically, i.e., they make it possible to record the overall dynamics of circulation as a sum of all such processes in all vessels of a cerebral region whose boundaries are known. However, other methods make it possible to localize regions functionally, i.e., to observe a specific branch (or its part) of the cerebral vascular system.

The recording response plays a large role in the investigation of processes within the intracranial circulatory system. This response is determined by the

minimum and the maximum rate of the process capable of being recorded by means of a particular method. The response of a method is conveniently expressed as the frequency range (in Hz) over which the recording of the changing processes is carried out without distortion. In this connection it should be noted that the maximum rates of change for processes in the vascular system (the harmonics of certain forms of pulse oscillations) correspond to frequencies up to 100 Hz, while the minimum process rates are close to 0 Hz.

Making use of these criteria, we shall further consider the basic methods used to study the physiology of intracranial circulation to show that the method of intracranial electroplethysmography selected by us is most suitable for investigating the mechanisms of compensation of blood volume changes in the cranial cavity.

Methods for local investigation of the cerebral vascular system.

Methods for local investigation of the intracranial circulatory system are of great interest because they give information on changes in the hemodynamic indicators for individual regions of the cerebral vascular system. However, the application of the majority of known methods to local investigation is accompanied by a disruption in the integrity of the cranial cavity and by a substantial injury to the animal, which limits their application. /16

Several methods are currently used for local investigation of cerebral circulation. Direct observation of cerebral blood vessels through a transparent window which replaces part of the cranial bone is one of the most common methods. Other common methods involve the use of roentgenoscopy with the introduction of substances into the blood which offer contrast to X-rays; and the recording of blood pressure and cerebrospinal fluid pressure in different parts of the vascular system. All these methods represent a direct method of investigation. Methods which make it possible to record the processes in the cerebral circulatory system indirectly are thermography and the electrical and magnetic recording of the blood flow rate in individual vessels.

The methods for direct observation of cerebral blood vessels have long been known. The observation of cerebral vessels through a transparent window in the cranium, first used by Donders, (1851) is still used successfully (Wolff, 1936; Alov, 1950; Klosovskiy, 1951; Mchedlishvili, 1959, 1962, Rosenblum and Lweifach, 1963 and others) and makes it possible to obtain a great deal of useful data. Modern microscopic techniques and mass microphotography have made this method sufficiently accurate and responsive. Its informativeness is quite obvious. This is still the only method which makes it possible to visualize the state of blood flow in surface cerebral vessels independently of their diameter.

The direct observation of cerebral blood vessels through a transparent window in the cranium is limited to surface cerebral vessels. This method cannot be considered to be sufficiently sensitive to resolve certain problems associated with intracranial hemodynamics. In particular, it does not make it possible to detect pulsation in a closed cranial cavity which, however, can be recorded by other methods.

Another method which permits the direct observation of cerebral vessels is angiography. This method makes it possible to visualize the blood flow in large cerebral arteries by means of roentgenoscopy after a substance providing for X-ray contrast is introduced into one of the arteries. Angiography makes it possible to measure, although with low accuracy, the diameter of large cerebral arteries and the rate of blood flow therein. In this technique sequential photography is used to observe the transport, by the blood flow, of X-ray contrast materials. De la Torre et al. (1959) used this method to observe the pulsation of cerebral arteries in a closed cranial cavity.

A significant advantage of angiography is that it makes it possible to /17
carry out observations on humans. Angiography in conjunction with photography, whose rate may be brought up to 24 frames per second through the use of contrast amplifiers, has been responsible for extensive data which have been obtained on the sequence of blood flow in different parts of the cerebral vascular system, as well as for data on the anomalies in the structure of the cerebral vascular system in man and in large laboratory animals (Curtis, 1949; De la Torre et al. 1959; Gal'perin, 1960; Grigorenko, 1960, and others).

The study of the effect of angiographic procedure on the test subject (Greitz, 1956; Sugar, 1961, and others) has shown that the substances offering contrast to X-rays are slightly toxic and their introduction into a blood vessel sometimes produces a change in its tonus depending on injection pressure and rate. All these factors, together with the insufficient resolving power of angiography, represent the basic shortcoming of this method and limit its possibilities.

The recording of pressure in vessels supplying blood to the cerebrum and in venous sinuses and cavities filled with the cerebrospinal fluid (CSF), may be achieved by various manometer systems. Until recently, pressure measurements were traditionally conducted with liquid-filled U-tube manometers. The values of blood pressures in blood vessels obtained by means of mercury manometers are close to each other. However, in most of the investigations, the scatter of data on the CSF pressure and its fluctuations under various conditions obtained by means of water manometers are rather wide. Thus, according to the data of O'Connel (1943), the CSF pressure in the lumbar cisterna of humans is equal to 400-500 mm of water, while according to the data of Becher (1922) it is equal to 30-180 mm of water. This discrepancy in measurement results may be explained by the fact that when a manometer is hooked up it causes pressure changes in a system. The likelihood of this proposition becomes obvious from the following discussion.

When a water manometer is connected to a system with volume V_0 initially filled with a fluid under pressure P determined by the stresses in the elastic walls of the system, part of the fluid which fills this system will be displaced into the manometer. This displacement will take place until the pressure of the liquid column in the manometer becomes equal to the pressure in the system. As result of this, the stresses in the walls of the system will decrease and the pressure in the system will drop by an amount ΔP equal to

$$\Delta P = \alpha \ln \left(1 - \frac{nS}{V_0}\right),$$

where S is the cross-section area of the manometer, n is the rise in the height of the liquid in the manometer, and α is the coefficient of expansion of the walls of the system. Since the volume occupied by the CSF is small, it is quite clear that the release of the CSF into the manometer when the latter is connected may change the pressure in the cranial cavity to some degree and thereby introduce a source of error. A similar idea has been expressed in the work of Ugryumov et al. (1957). Consequently, the absolute numerical data obtained in some of the investigations may be incorrect. This conclusion also pertains to various modifications of the manometric method--cerebral oncometry (Badmayev, 1958) and cerebral plethysmography (Avrorov, 1957). /18

This shortcoming of the water manometers can be eliminated completely by using electromanometers. These are being used more and more in the investigation of intracranial circulation. Electromanometers which are based on the use of tensiometric(Liberman, 1958; Antonov and others, 1961), mechanophotoelectric (Moskalenko, 1959) and variable inductance (Moskalenko, 1964) pressure transducers, exhibit a high sensitivity, a flat frequency response in the range from 0 to 150-200 Hz and a practically constant operating volume. Most recently, pressure sensors using semiconductor tensiometers have been more common. These are distinguished by small dimensions and high sensitivity.

The use of the piezoelectric effect for the transformation of pressure oscillations into electrical signals (Porye, 1946; Jacquet, 1951; Naumenko, 1957; Belekhova, 1958, 1959) makes it possible to design sensors for measuring the rate of pressure change which stresses the importance of phase relationships in recorders. However, this type of sensor does not make it possible to record processes which vary slowly.

The errors which appear when pressures are recorded by means of electromanometers are small and are due only to the instability of the recorders. It should be pointed out that in some works, for example in the monograph of Savitskiy (1956), it is pointed out that electromanometers used to record pressure generate larger errors than systems with mechanical recording of pressure due to distortions in the amplifiers. This may have been true to a certain extent ten years ago, but in our times most of the electromanometer systems are at least as good as the mechanical systems in all respects. As a rule, electromanometers give more accurate quantitative data on pressures in small cavities where the application of mechanical manometers is impossible.

Recently sensors based on the piezoelectric effect, which can used to evaluate indirectly the state of cerebral blood vessels, have been described. One such method is based on the recording of pulsations when the sensor is placed on the eyeball (Umanskiy, 1957), while in another the sensor is placed on cephalic skin (Pravdich-Neminskiy, 1950; Golland, 1960). Apparently data obtained with these two methods in some way reflect the state of the cerebrovascular system. However, it appears to us that they cannot be used to draw any conclusions concerning processes in the cranial cavity because the /19

reliability of the relationship between the recorded pulsation and the state of the cerebral vessels is unknown. Consequently, it is very difficult to evaluate the informativeness of such a method.

Among the indirect methods which are successfully used in the study of intracranial circulation we should first consider thermography. Versions of thermography are used to investigate the cerebral circulatory system. The first of these makes it possible to record the rate of flow in arteries which supply blood to the cranial cavity, while the second makes it possible to record the blood-flow intensity in the cerebral regions. The thermographic recording of the flow rate in large vessels, proposed by Rein (1928), is based on the recording of heat transfer by the flow of moving blood. This method has been used to obtain valuable data on changes in the flow rate in cerebral blood vessels under different states (Keller, 1930, 1939; Schneider and Schneider, 1934; Gibbs et al. 1934). In 1963 Klimovitskiy applied this method to study the special features associated with venous return from the cranium under the action of accelerations. The method of thermography gives only qualitative information on changes in flow rate because the biophysical analysis of this method (Katz and Kolin, 1938; Wever et al. 1956 and others) has shown that the temperature distribution in a moving blood stream is not uniform.

In 1933 Gibbs modified the thermographic method and adopted it for recording changes in the intensity of cerebral blood flow within bounded regions of the cerebral tissue (Gibbs, 1933). In this case the temperature-sensitive element which is heated by an electric current to a temperature which is one to two degrees greater than the temperature of the cerebrum is inserted into its tissue. When the heating power is constant the outflow of heat from the temperature element depends on the intensity of blood flow within the cerebral region surrounding the temperature element. Thus the temperature fluctuations of the sensor are proportional to the change in the intensity of the blood flow within the tissues which surround it.

In recent years this method has been modernized by using highly sensitive semiconductor thermistors and by the development of special approaches to the introduction of temperature-sensitive and heating elements into the cerebral tissue (Ludwigs, 1954; Blinova and Ryzhova, 1958, 1959, 1961; Parolla, 1959; Cooper, 1963, and others). When data obtained by means of thermography are analyzed it should be noted that the recorded changes of the total blood flow /20
intensity in the investigated region of the vessel or of the cerebral tissue do not yield well-defined data on the direction of the vascular reactions. Thus, for example, a decrease in the amount of heat carried away from the temperature element will be observed both in the case when the vessels constrict and when they undergo a sharp dilation accompanied by stagnation phenomena. It should also be noted that a substantial error can be introduced into the results by fluctuations of cerebral tissue temperature associated with the intensity of the metabolic processes. One of the merits of thermography is the fact that it makes it possible to geometrically localize the investigated cerebral region.

The selection of heater temperature plays a major role in the application

of thermography. On one hand it must be sufficiently high so that the temperature-sensitive element can record its maximum fluctuations while on the other hand the temperature of the heating must be as low as possible because the local heating of a cerebral region may in itself induce a change in the intensity of blood flow.

Suzuki and Motokawa (1965) proposed a new modification of the thermographic method which involves the heating of the thermistor by current impulses. This has made it possible to increase the accuracy of the method and to decrease its thermal effect.

The work of Betz (1965), which describes a modified version of thermography, is of interest. In this version the errors introduced by changes in the temperature of cerebral tissue and in its heat capacity are taken into account. Betz has shown that a change in heat dissipation produced by changes in the intensity of blood flow takes place in the cerebral region which is released by not more than 0.5 cm from the thermistor head and constitutes approximately 20 percent of the total heat removed.

The method of thermography is sufficiently sensitive. However, due to the low thermal response of the thermistor, the pulse changes in blood flow intensity recorded by this method may be distorted. Such are the advantages and shortcoming of the thermographic method for the investigation of cerebral circulation intensity.

In recent years electromagnetic methods for recording blood flow in intact vessels have been used. As is known, the blood flowing through a vessel has good electrical conductivity and represents a moving conductor which will generate induction currents in the presence of a magnetic field. Using this principle, Witterer (1937), Katz and Kolin (1938) developed special devices called current meters. Denison et al. (1955) improved the measurement technique and made it possible to record blood flow in small-caliber arteries--particularly in cerebral vessels.

The theoretical bases of this method which have only recently been developed rigorously (Wyatt, 1961; Kinai, 1965, and others) have shown that the nonuniform distribution of the magnetic field applied to the vessel and the complex nature of blood flow in the vessels introduces a large error into the measurement results which is very difficult to take into account. Wyatt has shown that when a number of technical problems have been resolved, this method can be used with great accuracy for the contactless monitoring of flow rate. /21

There is another method based on the peculiar electrical parameters of blood which is used to record the rate of blood flow. The principle behind this method consists of recording the changes in the electrical conductivity of blood during its motion. By using this method, Kedrov and Naumenko (1954) recorded the pulse changes of flow rate in jugular veins. Investigations on the theory of this phenomenon (Moskalenko and Naumenko, 1959b) have made it possible to establish the relationship between linear blood flow velocity and relative variation in the electrical conductivity of blood. When applied to intact vessels, this method gives only qualitative data in view of the complex velocity distribution of blood flow along the cross section of the vessel.

Weiman and Ben-Yaakov (1965) applied photoplethysmography to record changes in the blood volume of cerebral surface regions. The theoretical analysis of this method carried out in the Orlov monograph (1961) and in the article by Weiman and Ben-Yaakov shows that in principle this method can be used for the quantitative estimation of blood volume changes in body regions. However, the question of its applicability to the recording of blood volume in surface cerebral regions is still open.

One of the methods which makes it possible to obtain a certain amount of information on the state of blood flow in cerebral tissue regions is the method of electropolarography. This method gives some information on the dynamics of oxygen tension in cerebral tissue and is based on the measurement of a polarizing current between a point electrode inserted into cerebral tissue and a silent electrode. Special investigations have shown that the strength of current flowing between such electrodes, when a voltage from 0.4 to 0.9 volts is applied between them, is proportional to the oxygen tension in the cerebral tissue region surrounding the point electrode (Eskina and Yakovlev, 1951; Snezhko, 1956; Meyer and Hunter, 1957; Kovalenko, 1961, 1962; Cross and Silver, 1962; Cooper, 1963, and others).

Electropolarography, which provides for an overall evaluation of both cerebral tissue blood volume as the intensity of metabolic processes, may yield highly valuable information when used in conjunction with other methods.

Methods for general evaluation of cerebral circulation

The known methods for the general evaluation of the state of intracranial /22
circulation differ in a favorable manner from those considered in the preceding section by the fact that their application make it possible to keep the cranial cavity intact because the operations necessary to obtain the desired information are conducted through vessels which supply blood to and remove it from the cranium. For this reason methods of this type can be used to study certain problems associated with the physiology of intracranial circulation in man and also for the diagnosis of certain cerebrovascular system diseases.

In recent years there has been wide use of the method proposed by Kety and Schmidt (1945) for measuring the volumetric cerebral flow rate. This method is based on the Fick principle and consists of determining the arterioveneous difference in the nitrous oxide content of blood. The theory of this method developed by the above authors has made it possible to carry out a quantitative evaluation of volumetric flow rate in the cerebrum and has revealed the basic sources of errors associated with this method.

The Kety and Schmidt method has been the first to permit determining the absolute numerical values of cerebral volumetric flow rate in man and in large laboratory animals (monkeys, dogs, and cats). Subsequently this method was improved in relation to the technique of taking blood from the test subject (Scheinberg and Stead, 1949; Bernsmeier and Siemons, 1953, and others), which has made it possible to improve the accuracy of the measurements. However, the response time of the method still remains slow and the interval between measurements amounts to several minutes. The data obtained by this method also

make it possible to compute the total peripheral resistance of cerebral vessels as well as the oxygen consumption by cerebral tissue.

In recent years a new method of cerebral radiography based on the Kety-Schmidt method has been developed. This technique, which has made it possible to record similar indices, is free from the various shortcomings of the first method and therefore substantially simplifies the recording technique and improves its response time.

Cerebral radiography is achieved by saturating the blood with radioactive nitrogen (krypton-85) instead of nitrous oxide (Lassen and Munk, 1955; Lassen and Ingvar, 1961; Lassen, 1964) or by introducing substances into the blood which contain radioactive isotopes (Vasilevskiy and Naumenko, 1959; Eichorn, 1959; Thompson, 1961; and others).

The combination of radiography with the Kety-Schmidt method (Reinmuth, 1965) has made it possible to increase the recording time of blood flow up to one measurement per minute and to simultaneously determine the total cerebral consumption of oxygen and glucose. /23

On the basis of a large amount of experimental work, Ingvar and Lassen (1965) evaluate the radioactive method as the one most suitable for investigating human cerebral circulation.

The Kety-Schmidt method and its modifications involving the use of radioactive isotopes have made it possible to obtain valuable data on the variation in the relative cerebral flow rate during normal cerebral oxygen consumption and on the relative peripheral resistance of cerebral vessels with errors not exceeding 3-5 percent. Vasilevskiy and Naumenko (1959), who introduced substantial changes into the method of radiography, used it to measure the volumetric flow rate of CSF in the system of cerebral ventricles and to measure the flow rate through a system of cerebral vessels.

Another method of evaluating cerebral circulation is dynamography, which is based on the recording of the vertical load acting on regions of the human body. The variation in this load vary with the blood volume in the investigated body region (Babskiy et al. 1952). These investigators have shown that in some tests (particularly during high-level mental activity) blood volume is increased by 75-150 ml. However, the informativeness of this method is low because it is difficult to differentiate between the intracranial and extracranial vascular reactions, and also because it is difficult to take into account errors caused by involuntary movements and changes in the tone of the neck muscles.

In recent years, efforts have been made to study the system of intracranial circulation by using several methods which in the past have been used to study the peripheral blood flow. For example, this is done by using a method in which the dilution of an indicator introduced into the blood is determined. The theory of this method had been developed by Cropp and Burton (1966).

Another new method for the overall evaluation of the activity of cerebrovascular system is intracranial electroplethysmography[1], which is based on the recording of changes in electrical parameters between electrodes implanted into the cranial cavity. It is known that the different tissues of man and animal have a different electrical conductivity and dielectric constant (table 1). There is a particularly large difference between the fluid media of an organism (CSF, tissue fluid, blood, etc.) and the dense cellular tissues (muscle, nerve, bone, etc.). Therefore, any change in the amount of fluid in a particular region of the body or its organ is associated with changes in the electrical parameters. Thus, changes in the electrical parameters of a specific region of the body or its organ reflect fluctuations in the blood volume of associated vessels. /24

TABLE 1. ELECTRICAL CONDUCTIVITY OF SOME TISSUES, OF BLOOD, AND OF CSF (ACCORDING TO MOSKALENKO, 1959).

Test object	Electrical Conductivity (in ohm X cm) at different frequencies	
	100 Hz	1000 Hz
Muscle Tissue	700-1300	600-1200
Liver Tissue	800-950	700-900
Blood	125-200	120-190
CSF	60-80	60-70

Electroplethysmography, introduced at the beginning of the 20th century by Cramer, was first used by Kedrov and Naumenko (1954) to study cerebral circulation in animals. In recent years this method has been used to carry out a substantial number of investigations on the study of intracranial circulation in animals and in man (Beer et al. 1956; Moskalenko and Naumenko, 1957, 1958; Pratezi and Nuti, 1957; Antoshkina and Naumenko, 1960; Konovalova and others, 1961; Moskalenko and others, 1962, 1963, 1964a, 1964b, 1964c; Jenkner, 1962; Seipel et al. 1964; Yarullin, 1965; and others).

[1] This method is known by other names. For instance, American investigators call it "impedance plethysmography," while Austrian investigators call it "rheography." A modification of this method designed to record pulse waves when electrodes are placed on the skin in man, is called "rheoencephalography." Certain investigators are trying to establish a difference between "rheography" and "rheoplethysmography." It appears to us that this diversity in the terminology introduces a certain amount of confusion. Therefore, we retain the name given this method by Kedrov and Naumenko (1954), who used it to make the fundamental investigations.

At present, the methodological basis for intracranial electroplethysmography is being developed in two directions. One of these trends consists of a study of blood volume dynamics regardless of the rate associated with the record processes; the second direction, which has recently been called "rheoencephalography," consists of recording only the periodic fluctuations in blood volume of the cranial cavity. Therefore, rheoencephalographs, which are presently produced by several firms ("Gallileo," "Al'var" and others), record processes which have a lower frequency limit of 0.4 Hz.

The advantage of modified electroplethysmography is that when the lower frequency of the spectrum is limited, it is possible to design instruments which /25
can be used without constant adjustment, i.e., there is practically no limit to the duration of blood volume fluctuations which can be recorded. There is also a lesser effect on the results produced by the displacement of electrons during the motion of the test object. In several cases, in particular during prolonged experiments under conditions of a changed gravitational field, the special features of the method are of great significance. However, this modification of electroplethysmography makes it possible to exclusively record pulse waves without distortions. This situation substantially lowers the informativeness of the method, which would be higher if the frequency response of the device started with 0 Hz.

The first trend in the development of intracranical electroplethysmography is free of this shortcoming. However, when electroplethysmograms (EPGs) are recorded over a range starting from 0 Hz, errors are generated due to changes in the electrical parameters of living tissues which are not associated with the blood volume. This in turn limits the time for the continuous recording of the EPG. Thus, in recognizing the overall advantage of the first modification of electroplethysmography we should point out that in some investigations the second modification of this method is more suitable.

In summarizing the possibilities and limits of application of existing methods for the investigation of the intracranial circulatory system, we can see that each method in itself makes it possible to obtain data on only specific characteristics associated with the activity of the intracranial circulatory system. Such characteristics include: 1) the general or local intensity of cerebral flow, which is investigated by means of thermography and the analysis of gas contents, by the method of dilution and by electric and magnetic methods of measuring the flow rate in arteries supplying the brain with blood; 2) the tonus dynamics of individual vessels of the pia mater and of the regional cerebral arteries, which can be investigated by direct observation including angiography; 3) the dynamics of blood pressure in major arteries and in cerebral veins as well as the CSF pressure investigated by means of manometry; 4) the dynamics of cranial blood volume and of its individual components investigated by means of intercranial electroplethysmography, photoelectroplethysmography and to some extent by the isotope method.

Thus, each of the above groups of methods has relatively narrow possibilities. Therefore, an important condition for obtaining results from specific investi- /26
gations is the compatibility of the method (or of several complementary methods) with the problems which a specific investigation must solve. This requirement

is not limited to investigation of the intracranial circulatory system. Sometimes, however, in view of the complexities associated with the investigation of this region of the vascular system, an incompatibility between the purpose of the investigation and the method leads to distortions and incorrect conclusions.

It is obvious that the last group of methods is most suitable for solving the problem formulated in the present book--the study of the compensatory mechanisms of changes in intracranial blood volume. Also, intracranial electroplethysmography should be preferred as being the most informative and most accurate and having the best response time of this group.

Intracranial electroplethysmography is one of a group of indirect methods for observing processes in the cerebral vascular system. This determines its advantages as well as its shortcomings. The basic shortcomings of electroplethysmography are errors due to effects on electric parameters produced by substances in the cranial cavity and by processes unassociated with changes in its blood volume. It is also difficult to analyze the results quantitatively, which subjects this method to criticism and inhibits its wide application in laboratory and clinical investigations. In this connection we will consider the theory of electroplethysmography in the next section; we will show its basic advantages and disadvantages and also clarify the optimum biophysical conditions necessary for recording intracranial EPGs when the errors inherent in this method are minimized.

Section 2. The Theory Of Intracranial Electroplethysmography

The relationship of fluctuations in the electrical parameters of body or organ regions to the dynamics of their blood volume was established in the first investigations conducted with the aid of electroplethysmography (Mann, 1937; Kedrov, 1941; Nyboer, 1960), while investigations in recent years have shown the existence of a direct proportionality between changes in the electrical parameters of human body regions and their blood volume (Schwan, 1956; Nyboer, 1960 and others).

Investigations carried out to clarify the optimum biophysical conditions for the recording of blood volume dynamics (Schwan, 1956; Moskalenko, 1961, 1962b) have made it possible to establish the factors which determine the regions of the electromagnetic spectrum most suitable for recording EPGs of specific body regions and organs in man and animals.

There are other factors in addition to the magnitude of differences between the electrical parameters of blood and other tissues which affect the recording of EPGs. In low frequency ranges, aside from the magnitude of differences in the electrical parameters of the blood and other tissues, the electrode-tissue interface (electrical parameters of the epidermis) affects the EPG profile; at high recording frequencies, it is affected by the level of electrical field absorption in tissues as well as other factors. In both cases it is necessary to take into account the features of the biological effect of the electromagnetic field on the object.

When some of these factors are taken into account it is more expedient to record the EPG at low frequencies, while if other factors are taken into account it is more advantageous to conduct the recording at high frequencies.

However, if the effect of all of these factors is taken together, we conclude that only a few regions of the electromagnetic spectrum are suitable for recording EPGs.

The low frequency range (15-40 kHz) is most suitable for recording EPGs when the electrodes are placed directly on the investigated organ by-passing the epidermis. The recording of EPGs at low frequencies is desirable in acute and chronic experiments on animals and also for blood volume control during certain types of surgery on man.

The range of medium frequencies (100-150 kHz) should be used to record EPGs of human body regions when electrodes are placed on the skin.

The range of high radio frequencies (500-800 MHz) is used for the contactless recording of changes in the volume of different cardiac regions of man and in the depth of respiration under clinical and laboratory conditions.

The application of high frequencies in the recording of EPGs presents several definite advantages making it possible to record blood volume changes in deep human organs by passing a focused beam of radio waves through the investigated region of the body without making any contact with the body.

The advantages of the high-frequency electroplethysmography in the investigation of such organs as the heart and liver are obvious enough (Moskalenko, 1958), but the question of their advantages compared with that of low-frequency electroplethysmography in the study of the intracranial circulatory system still remains open. Therefore, we made almost no use of this modification of electroplethysmography in the investigations considered in the present monograph.

The optimum frequency range for recording EPGs in low-frequency ranges was established by comparing the averaged electrical parameters of two groups of objects such as blood or lymph and dense tissues (muscles, nerves, etc.). Therefore, the established frequency range should also be optimum when we use electroplethysmography to study the intracranial circulatory system. However, the recording of intracranial plethysmograms has a number of special features in contrast to the recording of EPGs of other body regions. The investigations of Kedrov and Naumenko (1954) have shown that the increase in the blood volume of the cranial cavity is accompanied by a decrease rather than an increase in its electrical conductivity, i.e., the change in electrical conductivity between electrodes implanted in the cranium when the blood volume changes has a sign opposite that in other regions of the body and in other organs. /28

The fluctuations in electrical conductivity between electrodes implanted bitemporally into the intracranial cavity are rather small and usually do not exceed 1.5-2.5 percent of the mean impedance between the electrodes.
In addition, the electrical conductivity of the cranial cavity, which was recorded by Kedrov and Naumenko (1954) at a frequency of approximately 300 kHz,

brain. This fluid has good electrical conductivity and serves as the main conductor of electric current.

The role of CSF as the main conductor of electrical current in the cranial cavity is confirmed by the distribution of the electric field between electrodes implanted into the intracranial cavity. These distributions show that the current density in spaces filled with the CSF is substantially greater than in the remaining regions of the cranial cavity (Moskalenko and Naumenko, 1956). This is also confirmed by measurement of dielectric losses (tan δ) between electrodes introduced into the intracranial cavity (fig. 2). Indeed, as we have shown in collaboration with T. T. Filanovskiy, the value of tan δ in this case is rather large and substantially in excess of tan δ for other organism tissues such as muscles (Aladzhalova and Maslov, 1957; Barbashova and Moskalenko, 1961; Filanovskaya, 1966). This fact shows that the main conductor of electrical current in the cranial cavity is a homogeneous ionic conductor rather than cellular structures. The CSF is such a conductor. It is interesting to note that the maximum value of tan δ for the intracranial cavity is obtained at frequencies of 20-40 kHz. This means that the optimum biological conditions for the propagation of the electric field in spaces filled with the CSF occur in this frequency range. /29

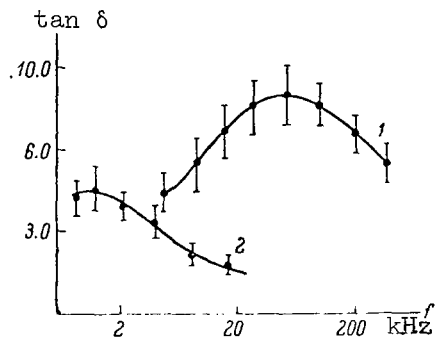

Figure 2. Variation in the dielectric loss (tan δ) function of frequency (f) when the electrodes are implanted into the cranial cavity (1), and when placed on muscle tissue (2). Results of measurements made on a cat under conditions of acute experiment. Vertical lines represent the 95 percent confidence intervals.

The fact that the frequency range of 20-40 kHz is the optimum one for recording intracranial EPGs is confirmed by data on the amplitude of periodic fluctuations in electrical conductivity between electrodes corresponding to the pulse variations in the blood volume of the cranial cavity obtained at different frequencies (table 2). The maximum amplitude of pulse fluctuations of the electrical conductivity is observed at frequencies of 20-40 kHz.

The maximum value of tan δ and the maximum relative amplitudes of pulse fluctuations in the electrical conductivity over the frequency range from 20 to 40 kHz confirm our proposition that this range is also the optimum one for recording EPGs of animals by implanting the electrodes into the cranial cavity. At the same time, the conclusion in regard to the key role of the CSF as the main electric current conductor in the cranial cavity makes it possible to explain the occurrence of changes in the electrical conductivity of the cranial cavity which are of opposite direction and which are associated with the dynamics of its blood volume.

TABLE 2. VARIATION IN THE AMPLITUDE OF THE INTRACRANIAL EPG PULSE WAVES IN DOGS AS A FUNCTION OF THE FREQUENCY (ACUTE EXPERIMENT)

Frequency (kHz)	Relative values of pulse fluctuations in the electrical conductivity of intracranial cavity (in percent of the mean value of electrical conductivity between electrodes).
1	0.020
5	0.030
10	0.035
20	0.040
30	0.050
40	0.045
60	0.038
80	0.032
100	0.028
150	0.022
200	0.020

Normally the volumes of blood in the pial vessels and the CSF which fills the subarchnoid space of the cerebrum are coupled. Therefore, increase in the blood volume of the cranial cavity will be accompanied by a decrease in the volume of the CSF and consequently by a decrease in the electrical conductivity between electrodes. On the other hand, when blood volume is decreased there will be an opposite change in the electrical conductivity. This was observed /30
by Kedrov and Naumenko as one of the special features associated with intracranial electroplethysmography. Thus, the intracranial EPG recorded by means of two bitemporal electrodes implanted in the cranial cavity reflects primarily the changes in the blood volume of the pial vessels. However, since part of the current passes through the brain tissue, the fluctuations in the blood volume of its deep sections also affect the recorded curve.

The special features associated with the propagation of electrical current in the cranial cavity make it possible for us to develop a quantitative relationship between changes in the electrical conductivity of the cranial cavity and the fluctuations in its blood volume. Let us conditionally represent the cerebrum with its surrounding membranes as a simple geometric model--a sphere with a specific electrical conductivity γ and two shells whose electrical conductivities correspond to the electrical conductivity of blood and of the CSF (γ_B and γ_F). We shall assume that the electrical conductivity of the cranial bones is substantially less, i.e., that the model is surrounded by a dielectric. In this case, the relationship between changes in the electrical conductivity of the cranial cavity and level of its blood volume is reduced to the establishment of a relationship for changes in the electrical conductivity of the model when there is a conjugate variation in the thickness of layers with electrical conductivities γ_B and γ_F.

In principle, this problem can be solved exactly because it pertains to the boundary value problems of electrodynamics. Its solution may be obtained in the form of series containing the eigenfunctions of the Laplace equation whose coefficients are obtained by matching the solutions at the boundary of the media. However, it is hardly expedient to carry out the associated cumbersome calculations because such a model represents an oversimplification of the true phenomena. We shall therefore limit ourselves to an approximate solution of this problem, assuming that the electric field in the diametric cross section of this model is uniformly distributed. This assumption is quite justified, at least with respect to the two surface layers whose electrical conductivities are close to each other and which carry a large part of the current.

In this case, if the electrodes are placed at the poles of the model, the overall electrical conductivity of the model γ which is established by integrating the electrical conductivity of the elementary volume of the model system of spherical coordinates, can be represented in the form

$$\gamma = \pi(\gamma_C R_C + \gamma_B R_B + \gamma_F R_F), \tag{1}$$

where γ_C, γ_B, γ_F are the specific electrical conductivities of the cerebral tissues, blood and CSF respectively; R_C, R_B, R_F are the distances of the layers' boundaries from the center of the model.

During the conjugate variation in the thicknesses of layers with electrical conductivities γ_B and γ_F by an amount ΔR, the variation in the electrical conductivity of the model will be equal to

$$\frac{\Delta\gamma}{\gamma} = \frac{\Delta R(\gamma_F - \gamma_B)}{\gamma_C R_C + \gamma_B R_B + \gamma_F R_F}. \tag{2}$$

Having established the volumes of layers with different electrical conductivities, it is easy to use equation (2) and obtain an expression for the relative change in the volume of a layer with electrical conductivity γ_B or γ_F /31

$$\frac{\Delta V}{V} = \frac{A\left(\frac{\Delta\gamma}{\gamma}\right) + B\left(\frac{\Delta\gamma}{\gamma}\right)^2 + C\left(\frac{\Delta\gamma}{\gamma}\right)^3}{R_0^3 - R_C^3}, \tag{3}$$

where A, B, C are constants which depend on the geometry of the cranial cavity while R_0 is the internal radius of the cranial cavity.

Proceeding from data on the specific electrical conductivity of blood, CSF, and cerebral tissues as well as from the geometry of the cranial cavity, relationship $\frac{\Delta V}{V} = f\left(\frac{\Delta\gamma}{\gamma}\right)$ may be represented by a curve, as shown in figure 3.

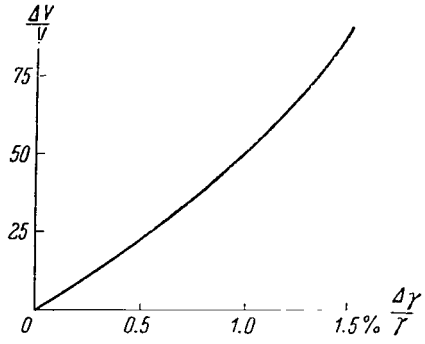

Figure 3. Variation in the relative changes of blood volume ($\Delta V/V$) as a function of the cranial cavity electrical conductivity changes ($\Delta\gamma/\gamma$). Calculated data.

This curve shows that the relative changes in the electrical conductivity of the cranial cavity and in its blood volume are directly proportional to each other over wide limits of blood volume changes in the cranial cavity. This is well confirmed by experimental data which were obtained during studies on changes in blood volume of the cranial cavity under the action of longitudinal gravitational stresses. In these experiments the variation in the blood volume of the cranial cavity as a function of the intensity of the stress was obtained by intracranial electroplethysmography and was in good agreement with computed results (Moskalenko and others, 1964b).

Although we made several assumptions in the computation process, the good agreement of measurement results with computed data indicates that the curve in figure 3 can be used to illustrate the relative changes in the blood volume of the cranial cavity based on the relative changes in the electrical conductivity between electrodes. It should be pointed out that this is possible only when the electrodes are sufficiently removed from each other (for example, if they are placed in different hemispheres) and their position in the cranial cross-section containing them is close to diametric.

Thus the relationship shown in figure 3 opens up possibilities for a quantitative analysis of the intracranial EPG. Such an analysis can be achieved after an experimental verification and refinement of equation (3). /32

The deviations in relationship $\frac{\Delta V}{V}=f(\frac{\Delta\gamma}{\gamma})$ from a linear one, when there are great changes in the blood volume of the cranial cavity, give a good explanation to the fact noted by Kedrov and Naumenko (1954) that the maximum changes in electrical conductivity of the cranial cavity are relatively small and approach only 1.5-2.5 percent of the mean value of the electrical conductivity between the electrodes.

In the preceding discussions we assumed that changes in the electrical conductivity of the cranial cavity are induced entirely by volumetric changes of the blood. However, substantial changes in the linear velocity of the blood flow are observed in the intracerebral vessels which according to the

data of Kedrov and Naumenko (1954) may also affect the electrical conductivity between electrodes, because the electrical conductivity of blood changes during its motion. This phenomenon was established by Sigman et al. (1937). They established that the electrical conductivity of circulating blood in a vascular system increases with the linear velocity of its motion. Somewhat later, Week and Alexander (1939) also observed the variation in the electrical conductivity of the blood column in the aorta of a rabbit when the blood flow was suddenly stopped.

A special investigation of this phenomenon (Moskalenko and Naumenko, 1959b) has shown that the electrical conductivity of blood varies, on the average, by 2-5 percent of its initial value when the linear velocity is increased from 0 to 15 cm/sec. The extent to which the electrical conductivity of blood changes during its motion is affected by the frequency of the current used to carry out the measurements (fig. 4) and by erythrocyte concentration in the blood. Experiments conducted with ionic and colloidal solutions, with a suspension of erythrocytes, and also with blood in which the erythrocytes were agglutinated to various degree, have shown that the basis for the changes in electrical conductivity of blood during its motion is the origin of a convection current due to the oriented motion of erythrocytes, which carry a negative electrical charge on their surface. /33

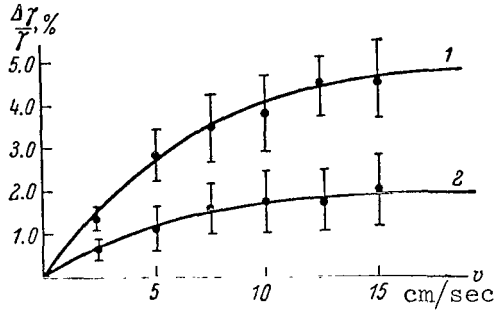

Figure 4. A variation in the electrical conductivity of blood ($\Delta\gamma/\gamma$) as a function of its velocity (v). 1. citrated blood at a frequency of 10 kHz; 2. citrated blood at a frequency of 100 kHz. The vertical lines represent the 95 percent confidence intervals.

On the basis of these data an expression was obtained which associates the relative change in the electrical conductivity of blood and its linear velocity:

$$\frac{\Delta\gamma}{\gamma} = \frac{qnv}{\left(\gamma_f + \frac{\varepsilon\omega}{4\pi}\tan\alpha\right)E + qnv}, \qquad (4)$$

where γ_f is the electrical conductivity of blood at rest, measured with dc current; E is the voltage between the electrodes; v is the mean linear velocity of blood; α is the angle between the vectors $\bar{E}$ and $\bar{v}$ under the assumption that the electrical field between the electrodes is linear; q and n represent the concentration and charge of the erythrocyte.

Recently Liebman et al. (1962) have established a relationship between the changes in electrical conductivity of blood and the velocity of its motion, basing their calculations on the change in the configuration of the electrical

field associated with erythrocytes during their motion. This approach to the problem, while making the calculations more complex, does somewhat improve the accuracy of the final expression compared with equation (6), particularly in the case when high frequencies are used.

The variations in the cerebral vascular blood flow rate are caused by the same reasons as those which produce a change in the blood volume. Measurements in vitro at a frequency of 30 kHz and calculations carried out by means of equation (6) show that when the blood flow rate changes from 0 to 15 cm/sec the change in its electrical conductivity is about 0.3 percent. If we take into account the nature of current distribution in the intracranial cavity this quantity becomes substantially smaller--no more than 0.5 percent; nevertheless, even in this case it is of the same order of magnitude as the relative variation in the electrical conductivity of the cranial cavity produced by fluctuations in the blood volume. Therefore, changes in the vascular blood rate also produce noticeable changes in the electrical conductivity between electrodes implanted into the intracranial cavity.

The variations in the electrical conductivity of the craniocerebral cavity due to changes in blood volume and in the blood flow rate have different signs. Specifically, if during cardiac systole the amount of cerebral blood increases, thereby producing a decrease in the electrical conductivity between electrodes, the increase in the flow rate of cerebral vessels simultaneously leads to an increase in the electrical conductivity between electrodes.

Thus, intracranial electroplethysmography reflects comprehensively both the changes in the flow rate as well as in the blood volume. In other words, we have the following expression /34

$$\frac{\Delta\gamma}{\gamma} = \frac{\Delta\gamma}{\gamma}_{\text{vol}} - \frac{\Delta\gamma}{\gamma}_{\text{m}}.$$

The quantities $\frac{\Delta\gamma}{\gamma}$ vol and $\frac{\Delta\gamma}{\gamma}$ m, as shown above, depend on the frequency used to record the EPG. It is therefore important to follow the dynamics of the variation in this quantity as a function of frequency used to carry out the measurements. By representing the variation in these quantities and their ratio as a function of frequency (fig. 5), we can see that if we do not consider the change in blood flow velocity when carrying out measurements at low frequencies, the error which appears does not exceed 10 percent. On the other hand, when measurements are made in the range of medium frequencies the error reaches a value of 50 percent. It follows that it is expedient to use low-frequency currents to record the intracranial EPG. In this case the magnitude of the error due to changes in the flow rate will have a minimum value.

Obviously, this conclusion is valid for the case when the electrodes are introduced directly into the cranial cavity before coming in contact with the dura mater. This can be achieved under conditions of acute and chronic experiments on animals. This case must also be considered when performing investigations on humans with electrodes implanted in the cranial cavity for the purpose of treating certain diseases (Crow et al., 1961). /35

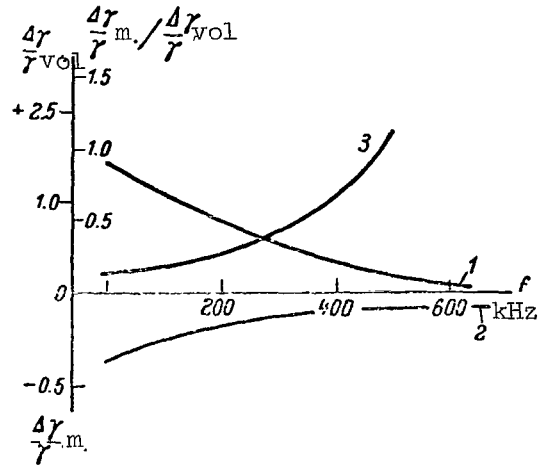

Figure 5. Variation in the electrical conductivity of the cranial cavity during a change in the blood volume ($\frac{\Delta\gamma}{\gamma}$ vol) and during a change in the cerebrovascular flow rate ($\frac{\Delta\gamma}{\gamma}$ mat) and the variation in the ratio of these quantities as a function of frequency (f). 1-$\frac{\Delta\gamma}{\gamma}$ vol due to volumetric change; 2-$\frac{\Delta\gamma}{\gamma}$ m due to velocity change; 3-$\frac{\Delta\gamma}{\gamma}$ vol/$\frac{\Delta\gamma}{\gamma}$ m.

Low-frequency electroplethysmography can be used to study certain problems of intracranial circulatory physiology in different classes of vertebrates. In order that the results obtained in experiments on animals of different size be comparable, it is important to maintain the same electric field distribution in the cranial cavity. This can be achieved by properly selecting the dimensions of electrodes implanted into the cranial cavity: experiments have shown that the maximum permissible diameter of disk electrodes must be not less than 15-20 times less than the internal perimeter of the cranial cavity transverse section in which the electrodes are implanted. The minimum diameter of electrodes is determined by the polarization phenomena whose role increases as the electrode area is decreased.

When analyzing the intracranial EPGs obtained in experiments on cold-blooded animals, it should be noted that the free-ion content in the blood of these animals is less than in the blood of mammals. This means that the relative changes in the electrical conductivity of the cranial cavity in cold-blooded animals compared with those of mammals will be greater for identical relative changes in the blood volume. It should also be noted that the relative volume

of the CSF in the cranial cavity of various animals is not the same and in some animals, for example in birds, the CSF is completely absent. This situation affects not only the magnitude but also the sign of changes in electrical conductivity between electrodes.

The modification of intracranial electroplethysmography considered above, which uses electrodes implanted into the cranial cavity, is not the only possible means of investigating the intracranial circulatory system with this method. Many investigations are known in which the recording of the intracranial EPGs in man was accomplished by placing electrodes on the skin of the head.

A number of authors (Donzelot et al., 1951; Beer et al., 1956; Eninya, 1962, 1965; others) placed electrodes on the temples of the subjects in order to record the pulse fluctuations in the cranial cavity. These investigators thought that an ac current of sufficiently high frequency would pass without hindrance through the cranial bones. However, these authors do not present any evidence to support their reasoning. Some studies have been published in recent years (Konovalova et al., 1961; Jenkner, 1962; Seipel et al. 1964; others) in which pulse fluctuations in the human intracranial EPG were recorded by placing the electrodes near /36 the natural openings in the cranium or in those places where the bone is least thick.

The biophysical phenomena which occur when the electrodes for the recording of EPGs are placed on the skin of the head can be simulated by a simple equivalent scheme in which the electrodes are represented by a condenser containing a stratified dielectric between the plates. When the electrical parameters of any layer of this dielectric change, there is a change in the capacity and in the Q (quality factor) of the condenser formed by the electrodes placed on the skin of the head.

Roughly speaking, we can distinguish four layers in the dielectric material contained between the electrodes; they correspond to the epidermis, the subcutaneous cellular tissue, the cranium, and the subarachnoid space filled with CSF.

These layers are arranged in a concentric manner around the central part of the dielectric, which consists of the brain tissue (fig. 6). Some of these layers are good conductors of electrical current while others are poor conductors. The equivalent circuit for this model is shown in figure 7.

The capacitances of the end cells C_{KK} are flat condensers formed /37 by the electrode and the subcutaneous cellular tissues. The dielectric material of these condensers is the epidermis, whose shunt resistance is represented by R_K. The second pair of RC networks is formed by capacitances C_{KL} whose plates consist of the cellular tissue and the layer of CSF contained in the subarachnoid space while the dielectric is the cranial bone with a shunt resistance R_{KC}. The CSF, which has a large but finite conductance, may in turn be represented in the form of a condenser C_L whose plates are the two hemispheres

such that the interval between them is filled with a dielectric material consisting of cerebral tissue with a shunt resistance R_M.

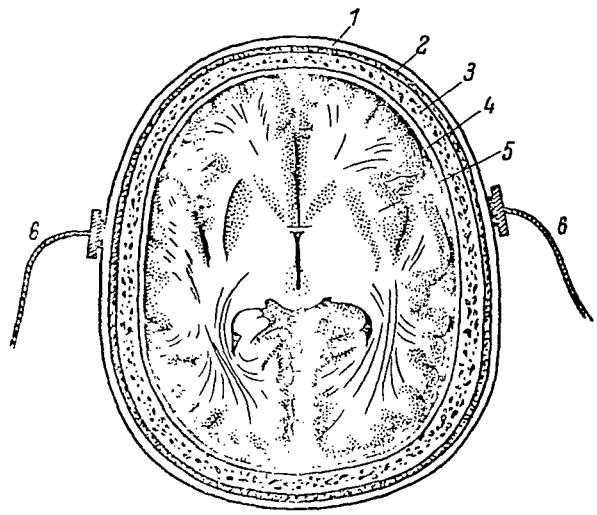

Figure 6. Schematic representation of tissues between electrodes when these are placed on the skin of a man's head. 1. skin; 2. cellular tissue; 3. bone; 4. space filled with CSF; 5. cerebrum; 6. electrodes.

This equivalent circuit can be reduced to a simple RC cell with parameters C_{eq} and R_{eq} by converting the parallel shunting resistances into series resistances and then adding the resistances and capacitance connected in this manner.

By assigning to the parameters of the circuit equivalent increments which simulate the extra- and intracerebral vessels, we can compare the changes in C_{eq} for the same relative changes in the blood volume of extra-and intracranial /38 vessels;

$$\frac{\Delta\omega'}{\Delta\omega''} = \sqrt{\frac{\Delta C'_{eq}}{\Delta C''_{eq}}} = 1.34.$$

Here $\Delta C'_{eq}$ is the variation in C_{eq} due to deviations in C_{KK} and C_{KL} or in the extracranial factors while $\Delta C''_{eq}$ is the variation due to the deviations in C_L or due to the intracranial factor.

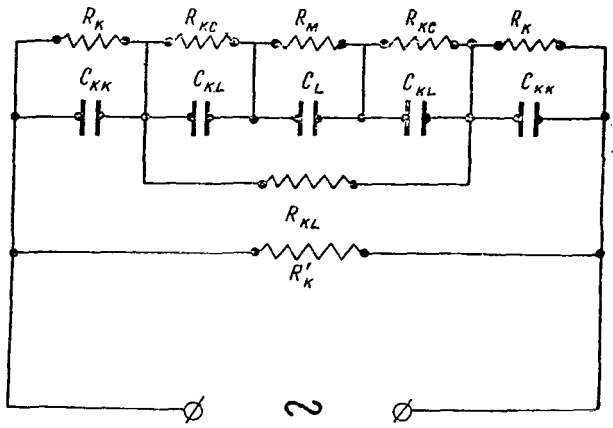

Figure 7. An equivalent circuit for the one formed when electrodes are placed on the skin of the head. R_K and C_{KK} are the resistance and capacity of the epidermis; R_{KC} and C_{KL} are the same for the cranial bone; R_M and C_L are the same for the cranial cavity matter; R_{KL} is the resistance of pia mater surrounding the cranium; R'_K is the surface skin resistance.

Since the principle of recording changes in C_{eq} by means of devices operating at high frequencies (Donzelot et al., 1951; Beer et al., 1956) consists of recording the resonant frequency of the oscillatory circuit containing the subject, the ratio of frequency changes in this circuit due to deviations in C_{KK} and C_{KL} on one hand and in C_L on the other will be equal to

$$\frac{\Delta C'_{eq}}{\Delta C''_{eq}} = 1.8.$$

Devices which utilize the bridge principle of measurement (Eninya, 1962, 1965; and others) are also sensitive to fluctuations in R_{eq}. It is easy to see that the ratio of changes in resistance $\Delta R'_{eq}$ on one hand to $\Delta R''_{eq}$ on the other will be greater than unity.

Thus, when recording the intracranial EPGs by means of electrodes placed on the temples, the error due to the same increment in the blood volume of intracranial and extracranial vessels is found to be of the order of 50-70 percent. When intracranial EPGs are recorded by the bridge method, at lower frequencies the principal error will be due primarily to changes in R_{eq}, in which case the total value of the error will be of the same order.

These considerations show that the main error in the recording of intracranial EPGs in man is due to C_{KK} and C_{KL}, whose dielectric materials are the epidermis and the cranial bones. We might be able to decrease the first capacitances, treating the skin with special pastes or by some other method, but we cannot control the value of C_{KL}. Therefore, it is of great interest to consider other variations in the placement of electrodes on the human head where the effect of these capacitances can be decreased.

One such version is the placement of electrodes near the natural openings in the cranial bone. If one binary electrode is placed on the eyes of the test subject while the second is placed in the region of the foramen occipitale magnum (fig. 8), we eliminate or substantially reduce the effect of capacitances C_{KL} and C_{KK} on the quantities C_{eq} and R_{eq} because the current flows into the cavity through natural openings and also the contact of one electrode is not with the epidermis but rather with the conjunctiva of the eye, which has a higher electrical conductivity. With this electrode arrangement the equivalent circuit is substantially simplified because we can eliminate the two C_{KL} and the C_{KK}. For this reason the ratios $\frac{\Delta R'_{eq}}{\Delta R''_{eq}}$ and $\frac{\Delta C'_{eq}}{\Delta C''_{eq}}$ are substantially decreased in value. It is easy to calculate that in recording the EPG the error produced by extracranial vessels is 10-15 percent in this case because the electrical current paths pass through the natural openings in the cranium and the poor electrical conductivity of the cranial bones has almost no effect on the EPG.

/39

Proof that our discussions concerning the above method of improving the efficiency of intracranial electroplethysmography in man are valid may be found in the work of Gilyarovskiy et al. (1953), who used direct measurements on rabbits to show that the maximum current density in cerebral superifical layers is observed when the electrodes are placed on the eyes and on the occiput of the animal. Another proof of this was obtained by Agte (1966), who showed that with the oculo-occipital position of the electrodes the compression by a cuff of the cutaneous vessels of the head has no effect on the pulse waves of the EPG recorded.

In another widely used method the positioning of the electrodes (Jenkner, 1962; Seipel et al., 1964; and others) is such that one of the electrodes is placed on the eyes of the test subject while the other is placed at the mastoid, where the resistance of the cranial bones has a minimum value. In this

case the errors in recording the intracranial EPG will be somewhat greater but still acceptable. The work of Seipel et al. presents proof that with this positioning of the electrodes the changes in the electrical conductivity between /40 them reflect the pulse changes, chiefly in the intracranial blood volume. Thus, in patients who, according to angiographic observation, have an occlusion of one of the internal carotid arteries, the pulse waves of intracranial EPG decrease substantially in amplitude when the common carotid artery on the other side of the neck is compressed. At the same time the squeezing of the common carotid artery from the side of the occlusion has no effect on the pulse waves of the EPG. If the recorded curve had reflected the pulse fluctuations of blood volume in the extracranial vessels, the compression of the common carotid artery from either side would have had the same effect on the dynamics of pulsation. The same results have been obtained recently by Collan and Namon (1965) with experiments on animals, where the electrodes were placed on the skin cover of the head.

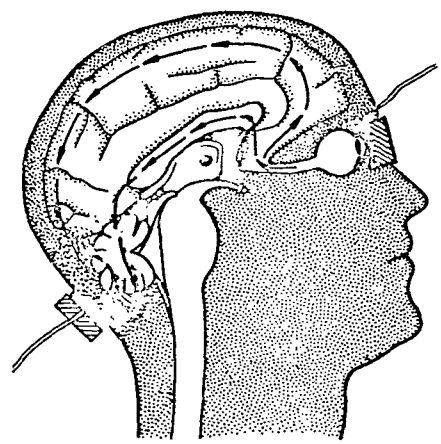

Figure 8. Schematic diagram showing the most efficient method of placing electrodes for the recording of intracranial EPG in man. The arrows show the path of the electrical current.

In any variation of recording the intracranial EPG in man, at least one of the electrodes is placed on the skin cover of the head. Therefore, the results of a recording are affected by changes in the electrical conductivity of the epidermis. An enormous amount of work has been performed in the last 50 years to study the resistance of the epidermis and its variations under different conditions. The resistance of the epidermis was studied when the method of galvanic skin reflex was developed (Richter, 1929; Spiegel and Wohl, 1935; Gorev, 1947), in the study of sympathetic innervation (Albrecht, 1921; Regelsberger, 1930) and also under different physiological states--sleep, digestion, etc. (Levine, 1930; Davydov, 1941; Ryvlina, 1941). The role of individual structural formations in the shaping of skin resistance particularly of the sweat glands, has also been studied (Yanusov, 1937; Mishchuk, 1948). The results of these investigations show extreme lability in the resistance

of the epidermis, whose variation in a series of cases may serve as an indication of various pathological states. However, in electroplethysmography this variability in the skin resistance may introduce a substantial error into the observed results.

The application of special methods to treat the skin, as shown by Vodolazskiy (1960), substantially reduces the resistance of its epidermis but still to an insufficient degree. Therefore, when recording EPGs, in order to decrease the resistance of the horny layer it is necessary to increase the operating frequency in addition to subjecting the skin to special treatment. This frequency used to record the EPG must be higher than that used when the electrodes are implanted into the cranial cavity. In other words, the recording must be made in the range from 100 to 150 kHz which is the one used to record EPGs of other regions of the human body.

It has been shown experimentally that an increase in the frequency to 100-150 kHz, when recording an EPG, together with the use of automatically wetted electrodes (Granat and Moskalenko, 1965), makes it possible to practically eliminate the effect of changes in electrical parameters of the epidermis on the results of intracranial EPGs in man when electrodes are placed on the skin of the head. /41

One other source of errors occurring during the recording of the intracranial EPG is due to changes, unassociated with the blood volume, in the electrical parameters of organism tissues. This includes changes in the electrical parameters of the cerebral tissues associated with the processes of metabolism, the development of their edema or dehydration when the composition of the blood of the CSF changes, etc. Undoubtedly, all these factors must be considered when recording the intracranial EPG.

In analyzing the factors which affect our selection of the optimum electromagnetic spectrum for recording the EPG we mentioned polarization phenomena.

In the regions of the electromagnetic spectrum selected by us, the capacitance component of the impedance between the electrodes implanted into the cranial cavity is small and averages $\sim$1000 mmf when the electrode area is not less than 0.1 cm^2. This means that the polarization phenomena at the interface between the electrode and the tissue are practically absent in this range of frequencies. This situation removes all limitations in regard to the area of the electrodes and to the metal from which they are fabricated. In selecting the design of the electrodes we should only ascertain that their introduction into the cranial cavity produces minimum injury to the test subject and that the metal is inert with respect to the surrounding medium.

When electrodes with an area less than 0.1 cm^2 are used, the indicator of an increase in polarization is the increase in the capacitive reactance between the electrodes or a decrease in tan δ.

The maximum time for the continuous recording of intracranial EPG is determined by two factors.

In the first place the total impedance of the brain, as shown by the investigations of Aladzhalova (1954) is subject to continuous oscillations associated with the processes of metabolism. The period of these oscillations is 30-60 min. Thus, changes in the impedance of the cerebral tissues may also affect the dynamics of the intracranial EPG level and may add up with changes produced by the dynamics of blood volume. In practice the changes of cerebral tissue impedance associated with metabolism produce a constant drift in the EPG zero level which becomes more pronounced as the time of continuous recording is extended. However, even with the presence of the drift background it is still possible to isolate the measurements of the intracranial EPG level produced by the vascular reactions over a period of several minutes (sometimes up to 15-20 min.). However, in order to establish the special features associated with the action of dc it is necessary to collect enough information so that a statistical analysis can be made. /42

In the second place, the level of the intracranial EPG is substantially affected by the artifacts associated with the motion of the animal and particularly with the displacement of the electrodes. The latter situation apparently takes place when intracranial EPGs are recorded in man. As a rule, in this case it becomes necessary to interrupt the recording and to adjust the equipment. The only way to eliminate these artifacts is to secure the electrodes and to make it impossible for the test subject to move when the EPG is recorded.

The biological action of the electrical current which has passed through fluid filling the cranial cavity is quite significant when the method of intracranial electroplethysmography is applied. Proceeding from the general concepts concerning the mechanisms associated with the action of the electromagnetic field on living tissue, we can say that in the range of lower radio frequencies, which is optimum for the recording of intracranial EPGs, the biological effect may be due to the stimulating action of ac current. Special experiments conducted to determine the threshold of sensitivity in the test subject at frequencies of 20-40 kHz when electrodes are implanted in the cranial cavity and at frequencies of 100-150 kHz when they are placed on the skin have shown that in the first case this threshold is 7-10 V while in the second it is 15-25 V. Therefore, to be certain that the undesirable effects of this type are absent we used a voltage 3 to 4 times less than the threshold values when recording the intracranial EPG. Inasmuch as the total impedance between electrodes in various experiments did not vary by more than a factor of 2, we can state with assurance that the current strength with these potential differences did not exceed the threshold value.

The data presented show that the method of intracranial electroplethysmography may be used successfully to record the dynamics of the cranial cavity blood volume both by implanting electrodes into the cranial cavity and by placing them on the skin cover of the head.

The method of electroplethysmography provides an almost instantaneous response and makes it possible to record both the slow changes in the blood volume of the cranial cavity (within certain limits) and very rapid changes, i.e., intracranial electroplethysmography has a low time constant. The relationship between changes on the EPG and changes in the blood volume of the cranial cavity are practically linear over a wide range. As we noted above (page 22) this proposition is valid in the case when the sensing electrodes are sufficiently removed from each other, for example when they are implanted bitemporally into /43 the cranial cavity of the animal. In the case when the electrodes are positioned on the surface of the cranium and are close to each other, or are introduced into the cerebral tissue, the changes in the electrical conductivity between them will reflect the blood volume dynamics of a certain region of the intracranial cavity where the maximum density of the electrical field is localized. By moving the electrodes closer together, this region may be made quite small and this in turn may be of interest in certain investigations. It is difficult to say whether in this case one will encounter the same relationships which are valid for two remote surface electrodes, but as shown experimentally (Kedrov and Naumenko, 1954; Antoshkina and Naumenko, 1960; Moskalenko et al., 1964c), the EPG recorded by means of two close electrodes permits qualitative evaluation of the blood volume dynamics of individual cerebral regions.

The recording of the intracranial EPG entails definite errors produced by the effect of processes unassociated with the dynamics of its blood volume, on the electrical conductivity of cranial cavity fluids. However, when optimum conditions are maintained for recording the intracranial EPG--optimum frequencies and voltage applied to the electrodes, a limited recording time or the adjustment of the equipment during a long experiment--then these errors are not large. By limitation of the frequency response of the recorded processes, the time during which a continuous recording of the EPG can be made may be substantially increased.

Electroplethysmography satisfies the requirements for measuring physiological processes under conditions of a variable gravitational field because it makes it possible to monitor the test subject remotely by means of a communication link. In this case the equipment installed with the test subject may be light-weight. It is therefore not an accident that in a recently published work by Akulinichev et al. (1964), electroplethysmography is classified as one of the promising methods in space physiology.

All that has been said above shows that intracranial electroplethysmography, in spite of its definite shortcomings, may be used successfully as the basic method for studying the mechanisms of compensation for changes in the blood volume in the cranial cavity under normal conditions and increased gravitation. However, it should be pointed out that the information on the dynamics of the cranial cavity blood volume obtained by electroplethysmography is not always sufficient to evaluate the entire complex of processes occurring in the intracranial circulatory system under increased gravity. This is so because intracranial electroplethysmography reflects only one side of the intracranial hemocirculation--the fluctuations in blood volume in the cranial cavity. For example, /44 this method does not give us sufficient information to establish the reasons which produce changes in the blood volume of the cranial cavity. Information

obtained by means of intracranial electroplethysmography is itself insufficient to evaluate the intensity of cerebral blood flow or the level of the blood supply to the cerebrum. All these factors serve as a significant shortcoming of this method. Therefore, in our investigations, depending on the specific purposes of the experiments, we recorded several other physiological indicators simultaneously with the intracranial EPG.

In many experiments additional information was obtained by recording the intracranial pressure and blood pressure in the arterial and venous systems of the cerebrum. The dynamics of pressures in these systems reflects the forces responsible for changes in the blood volume of the cranial cavity and consequently, significantly augments the data obtained by means of intracranial electroplethysmography.

Also, the simultaneous recording of these processes is interesting for other reasons. As shown by Landahl (1958), the simultaneous recording of the pressure of blood entering the cranial cavity and of the intracranial EPG yields information on the intensity of the cerebral blood flow. It is true that Landahl did not consider the conditions of venous release from the cranium, but this can be corrected by simultaneously recording the venous pressure or the intracranial pressure associated with it.

In some experiments we also recorded oxygen tension in the cerebral tissue (polarographic method) or some indicators for the state of the cardiovascular system (EKG, systemic arterial pressure, cardiac contraction rate, EPG of extremities and of the thorax, etc.).

Section 3. Recording Equipment and Investigation Technique

As we know, the description of the experimental technique is interesting from two points of view. First, it permits evaluation of the reliability of experimental data obtained by investigations performed with the particular method. In the second place, some aspects of the experimental technique may be interesting from the standpoint of their application in other works.

Recording Equipment

In our investigation of the intracranial circulatory system we used several designs of instruments for recording the intracranial EPGs and also for recording other characteristics of the test system. One of the devices, for example the galvanometric setup, used in the early stages of research (Moskalenko and Naumenko, 1956), is of no interest today. Other devices may be of interest /45
from the standpoint of their application in other investigations and therefore we describe them briefly.

Over the past few years several types of devices have been proposed for recording the blood volume of body regions and organs by means of electroplethysmography (Holzer et al., 1945; Kedrov and Naumenko, 1954; Fejfar and Zajitz, 1955; Polzer et al., 1960; Nyboer, 1960; Moskalenko, 1962; Kanai, 1965;

Arnautov, 1965; and other). They utilized three methods of recording changes in the total impedance. These methods are the potentiometric method, the bridge method and the four-electrode system for the input arrangement of electroplethysmographs (fig.9).

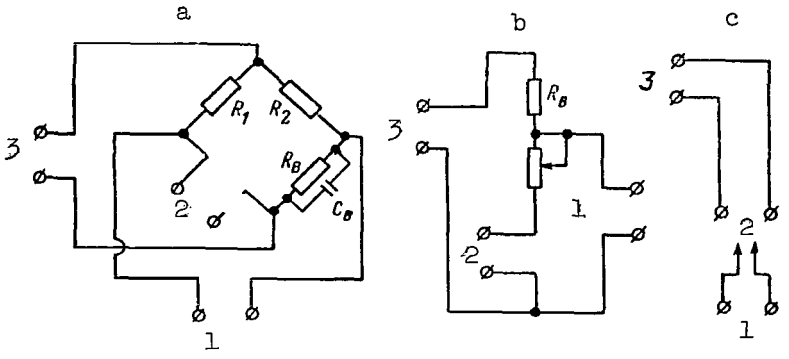

Figure 9. Schematic diagrams for the input devices of electroplethysmographs. a. bridge; b. potentiometric; c. four-electrode.
1. to generator; 2. to subject; 3. to amplifier

As we have shown above, changes in electrical conductivity between electrodes implanted into the cranial cavity are small and are substantially less than the changes in the electrical conductivity of other regions of the body due to the dynamics of their blood volume. Therefore, in order to record the intracranial EPG it is best to use instruments based on the bridge principle of measurement. The bridge circuit is used in the rheographic attachments to the electroencephalograph.

The general circuit diagram of the electroplethysmograph based on the bridge principle of measurement is shown in figure 10. The generator stage, which is tuned to a frequency of 20-40 kHz (for implanted electrodes) or to 100-150 kHz (for electrodes placed on the skin covers), must provide for a voltage of 3-4 V across a load of approximately one ohm. The harmonic content of the generated signal must not exceed 0.2 percent.

Much experience obtained by working with various types of EPGs has shown /46
that the bridge circuit, which makes it possible to carry out experiments on various types of animals, must provide for the balancing of the bridge over the range from 300 to 1800 ohms and from 500 to 2000 mmf. A satisfactory recording of the intracranial EPG is achieved when the signal measured at the bridge is amplified 5000 times. The signal then goes through a detector and through the output stages whose parameters depend on the type of recorder used.

The general block diagram shown in figure 10 was used as a basis to construct several versions of the electroplethysmograph. Good results were obtained by a setup consisting of standard laboratory instruments (the ZG-11

generator, MPP-300 impedance bridge, MVL-3 vacuum-tube voltmeter, the EO-7 and MPO-2 oscillographs). We used this setup both for investigations on animals and for observations on humans when the electrodes were placed in the oculo-occipital arrangement.

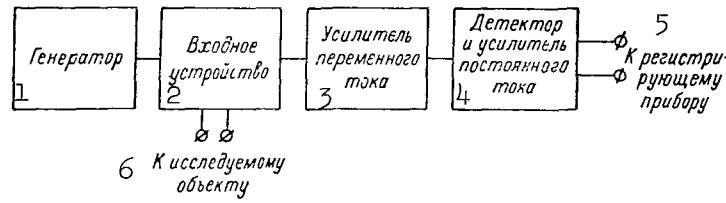

Figure 10. Block diagram of an electroplethysmograph with a bridge input circuit

1. generator
2. input device
3. ac amplifier
4. detector and dc amplifier
5. to the recorder
6. to the test subject

Two portable versions of the electroplethysmograph (Moskalenko, 1962), designed for carrying out investigations on large laboratory animals under increased gravitation, were developed. One of these devices was transistorized while the other used miniature tubes.

The first stage of the transistorized electroplethysmograph (fig. 11) consists of a sine-wave generator with inductive feedback, tuned to a frequency of 30 kHz. The buffer amplifier makes the output parameters of the generator independent of loading and matches the circuit to the internal impedance of the bridge. The bridge has a provision for controlling capacity over a range from 850 to 1000 mmf and balancing the resistance over a range of 700 to 1200 ohms. The carrier frequency is amplified by a two-stage wide-band amplifier whose total gain is approximately 2000. The amplification factor varies as a function of the input voltage. This makes it possible to observe, without additional adjustment of the device, both the major fluctuations in the blood volume--pulse /49 and respiratory waves, and the major changes in the blood volume, which result from some particular interaction. The output stage consists of a half-wave rectifier. The output voltage of the device varies from 0 to 6 V; the device is powered by a dc source of 24-27 V and consumes a current of 5-6mA. The device weighs 300 grams.

In the miniature-tube version of the portable electroplethysmograph (fig. 12), the generating stage consists of a 30-kHz master oscillator and a buffer amplifier. The amplifier has two stages L_3-L_4 and L_5-L_6, such that the gain of each stage is equal to 55. Frequency-sensitive negative feedback is introduced to eliminate noise. The output stage of the device consists of a

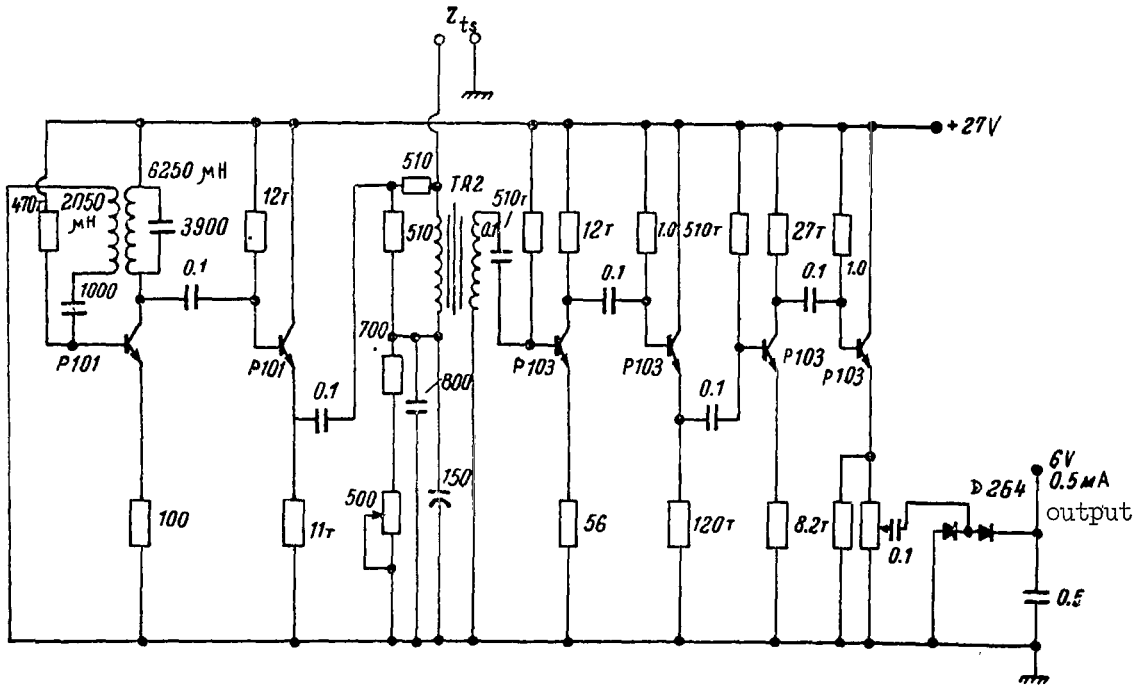

Figure 11. Circuit diagram of the portable transistorized electroplethysmograph. Z_{ts} is test subject.

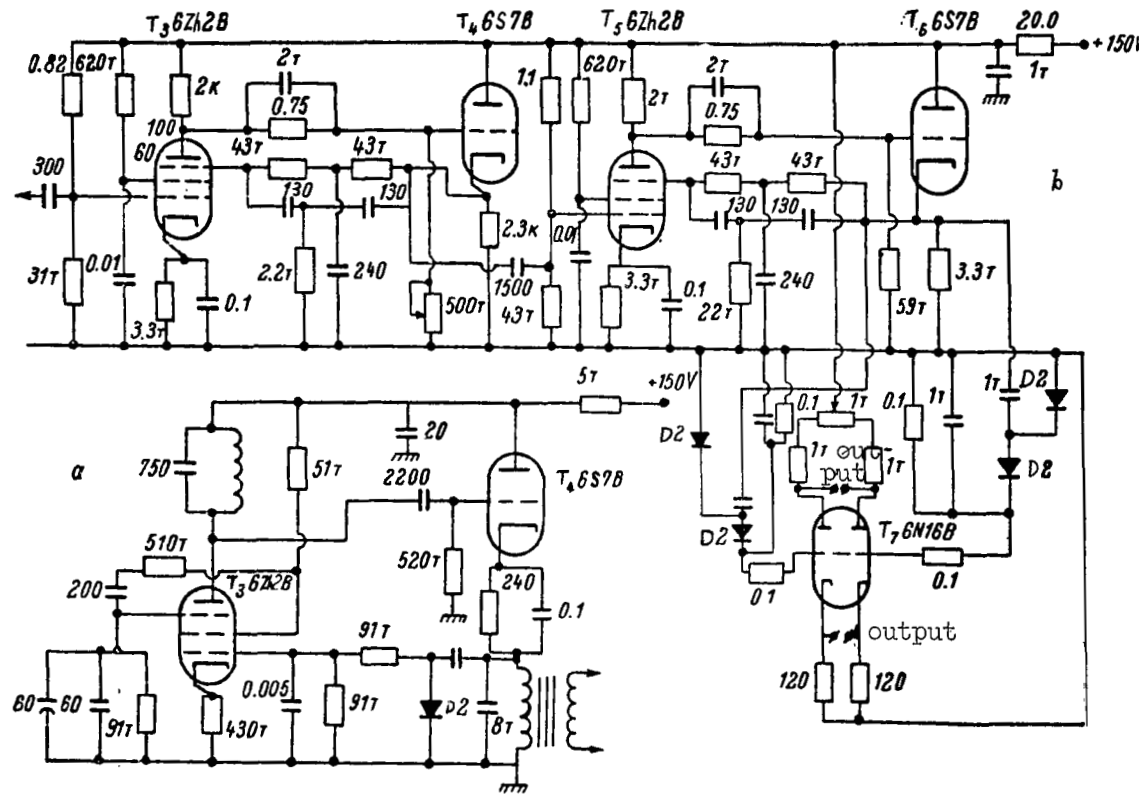

Figure 12. Circuit diagram of a portable electroplethysmograph utilizing miniature tubes. The input device is not shown.
a. generator; b. amplifier and output stage

detector and a power amplifier (L_7) designed to match the device of a low- or high-impedance recorder.

Recently a radiotelemetry system has been developed to record the intracranial EPG and intracranial pressure over a single radio frequency channel (Moskalenko, 1964). The first unit of this system (fig. 13a) consists of a modulator with a generator (T_1) tuned to a frequency of 35 kHz; the frequency of the generated signals is varied 5 percent by means of a variable-inductance pressure sensor. The generator is connected to the bridge circuit through the emitter repeater T_2. The frequency- and amplitude-modulated signal of the first stage is used to modulate the signal produced by the high-frequency generator tuned to 100 mHz ($T-T_4$) and which in turn telemeters the information to a distance up to 10 meters. The design of the generators in the first and second stages is based on a circuit proposed by Wolff et al. (1962). The total weight of the two sections together with the power supply is approximately 100 grams. The device is designed so that it can be attached to a freely moving animal (fig. 13b), but its electroplethysmographic channel was used to record the intracranial EPG in humans with electrodes implanted into the intracranial cavity.

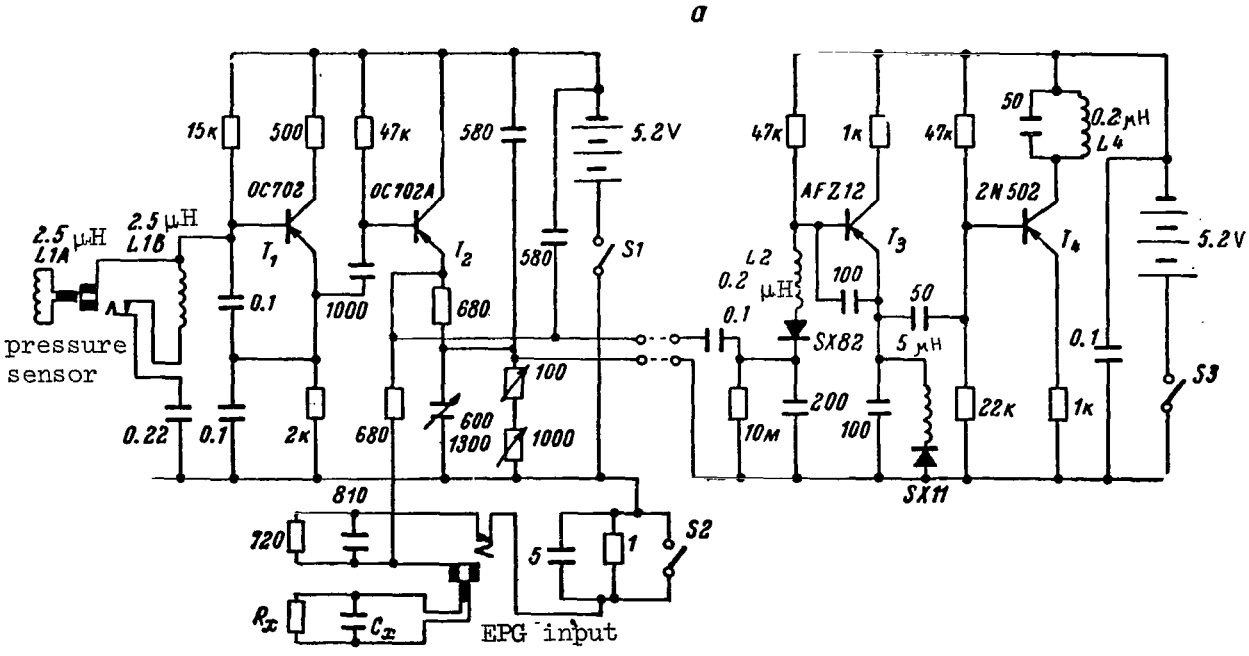

Figure 13a. Circuit diagram of the telemetering system for recording intracranial EPG and the intracranial pressure by means of a single channel.

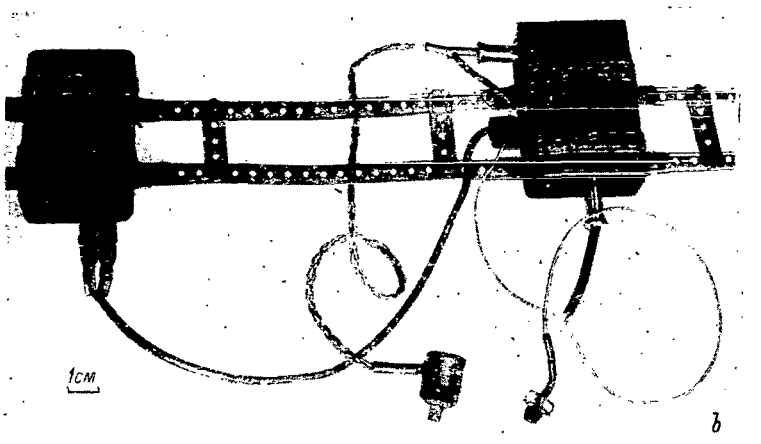

Figure 13b. External view of the telemetering system for recording the intracranial EPG and the intracranial pressure by means of a single radio channel.

The radiotelemetry signal, which can be received with a convential FM receiver, is fed from the output of the receiver to a demodulator (fig. 14) in which the amplitude-modulated signal (information on the intracranial EPG) is isolated by means of wide-band amplifier T_5-T_6, while the frequency-modulated signal (information on intracranial pressure) is isolated by means of a device consisting of an integral generator T_3-T_4 tuned to a frequency of 35 kHz and mixer T_7 which converts the 35±5 percent kHz signal into a 0 to 250 Hz signal. This is followed by two flip-flop stages T_9-T_{10} and T_{11}-T_{12} which convert the /51 frequency-deviation signal into a variable-frequency square-wave pulse of constant duration and amplitude. These pulses are in turn converted into voltages by means of a storage capacitance.

Recently the overall block diagram of the electroplethysmograph has been somewhat modified by the introduction of a phase-sensitive defector (Moskalenko et al., 1964a). The use of such a detector (fig. 15) makes it possible to eliminate one of the basic shortcomings of electroplethysmographs which use the bridge principle for recording changes in the electrical parameter. This undesirable feature is the nonlinearity of the volt-ohm characteristics near the bridge balance point (fig. 16), which makes it necessary to detune the bridge slightly in order to measure the EPG in a linear region. This had complicated the operation of the device. However, the high sensitivity of the bridge circuit has not been affected by these changes.

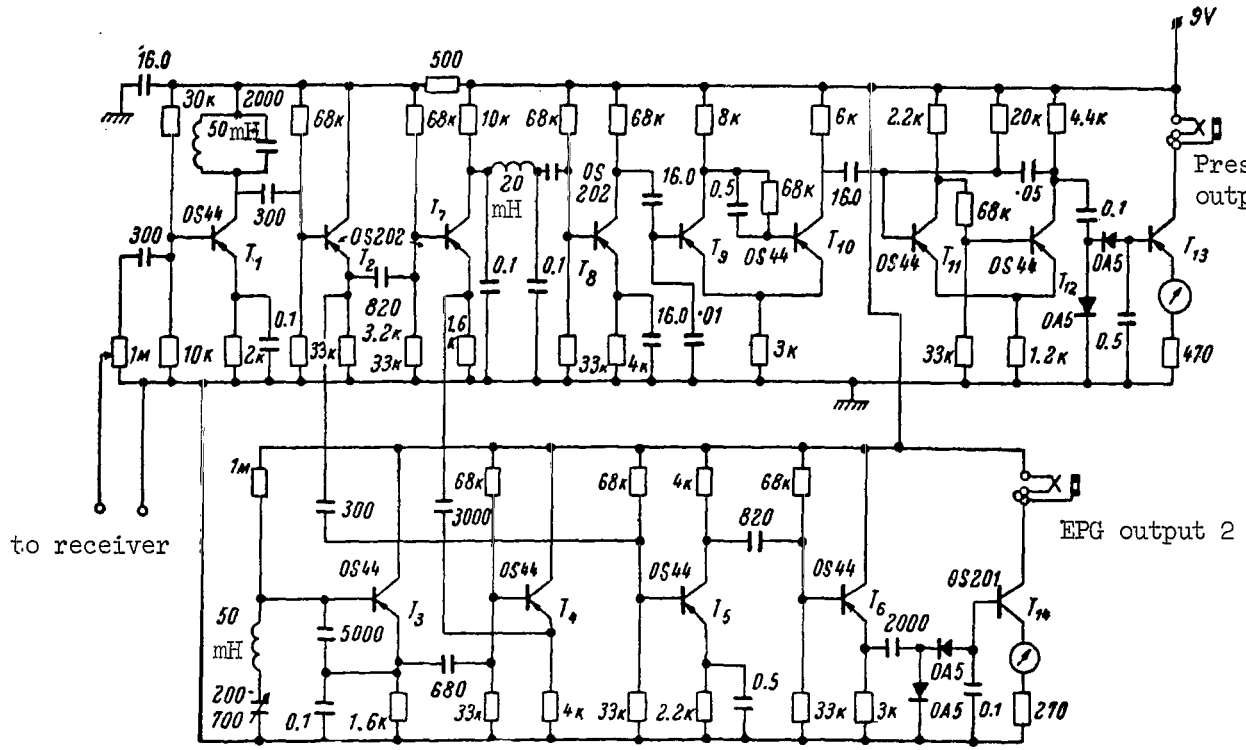

Figure 14. Schematic diagram of the demodulator for the telemetering system shown in figure 13.

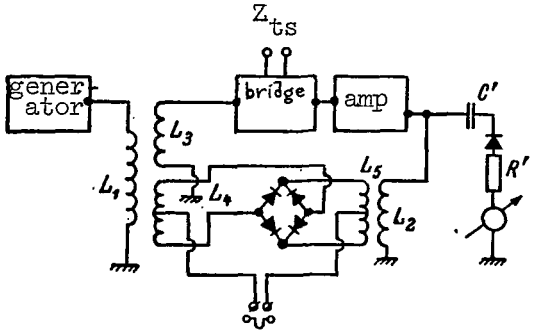

Figure 15. Block diagram of an electroplethysmograph with a phase-sensitive circular detector. Z_{ts} - test subject.

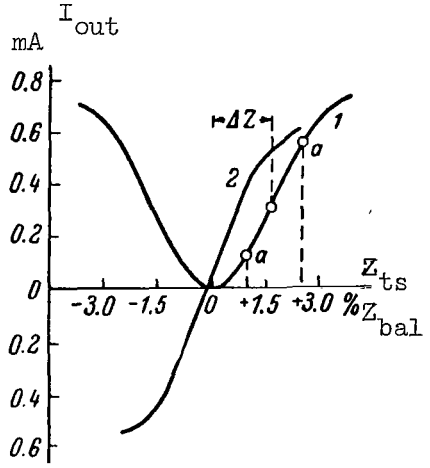

Figure 16. Relationship between the output current (I_{output}) of the electroplethysmograph and the ratio of the test subject impedance (Z_{ts}) to the impedance of the balanced bridge (Z_{bal}). 1. conventional bridge circuit; 2. circuit with a phase-sensitive detector; ΔZ the degree of bridge unbalance; aa. linear region of the characteristic.

Several devices for recording the level of intracranial pressure fluctuations pressure and of arterial and venous pressures were used simultaneously with devices used to record the intracranial EPG. This was done to obtain additional /53 information on the mechanisms of compensation of changes in the blood volume of the cranial cavity. Among such devices the mechanophotoelectric sensors (manometers) whose design is shown in figure 17 are of interest.

One manometer is designed for implantation into the cranial cavity of animals (fig. 17a), while the other two are designed for use under conditions of acute experiment (fig. 17,b,c). These manometers consist of a photoresistance 1 (or a photodiode); diaphragm 2, which is mechanically coupled to the elastic membrane 4; and a light source 3. When the membrane moves the diaphragm is displaced, which changes the illumination of the photoresistance. This change is recorded by means of a device operating on the principle of an electronic bridge (figs. 18, 19).

The manometer shown in figure 17c uses two light-sensitive elements such that the distribution of the light flux between them depends on the position of the diaphragm. The case of these manometers is made of plastic while the membrane is made of celluloid. The construction of the internal cavity of all types of electrometers which we used had a provision for extinguishing the pressure /54

waves reflected by the membrane. This prevented the distortion of the recorded curves when blood pressure and pulse waves of intracranial pressure were recorded. The sensitivity of the mechanophotoelectric pressure sensors was approximately 1 ma/1 cm H_2O, while the resonant frequency of the mechanical system was 200 to 400 Hz.

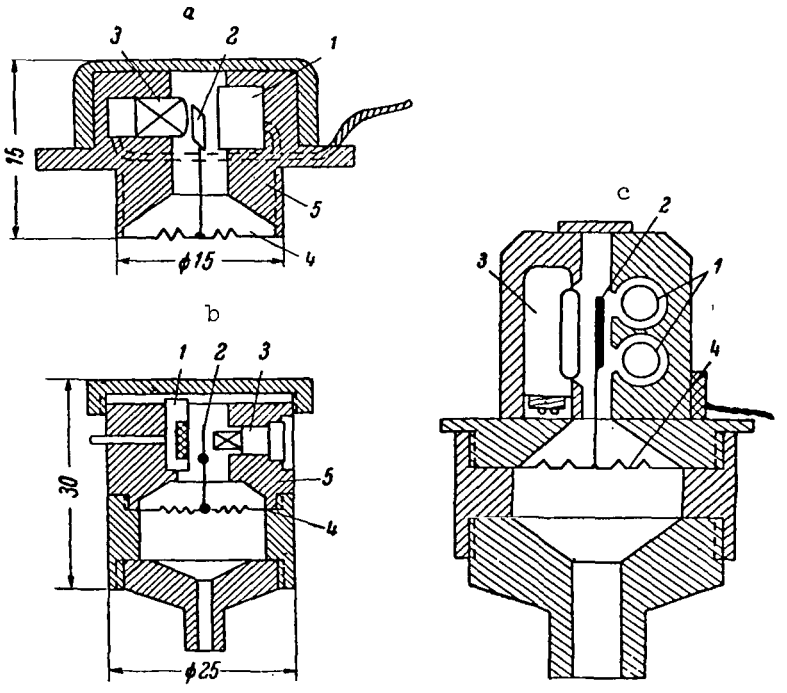

Figure 17. Design of the mechanophotoelectric manometers. a. sensor for implanation into the cranial cavity of dogs; b. sensor for recording pressure under conditions of an acute experiment; c. photoelectric pressure sensor with two light sensing elements. 1. photoresistance; 2. moving diaphragms; 3. light source; 4. membrane; 5. case.

We also used electromanometers based on the tensometric and variable inductance principles of mechanoelectrical transformation. The design of these manometers differs little from the design of known manometers of this type. We also investigated piezomanometers described by Naumenko (1957). We used piezoelectric manometers when it was necessary to record the rate of pulse pressure fluctuations, in order to measure more accurately the time interval between the initial instants of pulse pressure rise in different regions of the vascular system and when it was necessary to compute the pulse waves propagation rate. /55

In some experiments we have also recorded the oxygen tension in the cerebral tissue of animals using a device proposed by Kovalenko (1961). In the

case of humans we did this by using an attachment to the electroencephalograph (Cooper, 1963). Other auxiliary indicators, (sphygmogram, EPG, movement associated with respiration etc.) were recorded by conventional methods.

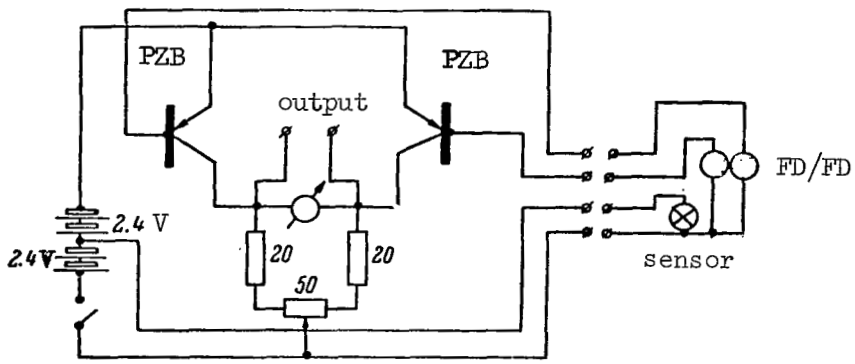

Figure 18. Electrical circuit of a device for recording pressure by the mechanophotoelectric manometer shown in figure 17c.

The combined recording of intracranial EPG together with the intracranial pressure and of blood pressure in different regions of the vascular system as well as of other physiological indicators enumerated above was achieved by using a setup which in addition to standard laboratory equipment used devices of original design. A block diagram of this setup is shown in figure 20. Figure 21 shows the physiological characteristics of the intracranial circulatory system which can be recorded together with arterial and venous pressures in any combination by means of the six operating channels in this set-up. /56

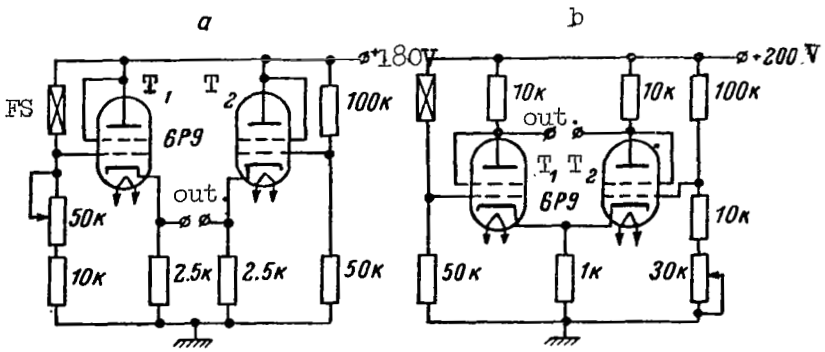

Figure 19. Electric circuit of a device for recording intracranial pressure by photoelectric manometers. a. circuit designed for attachment to a loop oscillograph; b. circuit designed for attachment to a cathode oscillograph; c. output of the device.

The mechanisms for the compensation of blood volume changes in the cranium was investigated in various objects by means of apparatus and devices described above. Most of the experiments were performed on large laboratory animals--dogs, and cats,--and rabbits, in which the entire combination of processes could be recorded as shown in figure 21. /57

In experiments on small laboratory animals--rats, pigeons, chickens, turtles, lizards and frogs-the respiratory movements and the sphygmogram were recorded together with the intracranial EPG.

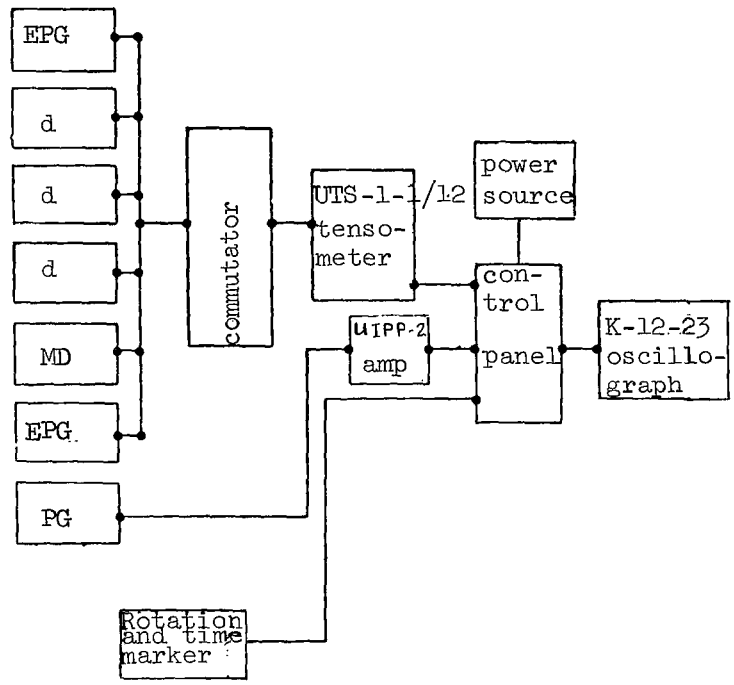

Figure 20. Block diagram of a 7-channel laboratory apparatus for investigating the intracranial circulatory system. d- pressure channel; PG - electropolarographic channel; EPG - electroplethysmographic channel; MD - channel for a chest mechanogram.

Experimental Technique

Intraperitoneal urethane anesthesia (1g/kg) was used in acute experiments on animals involved. It is of course impossible to say with assurance that this form of anesthesia had the same effect on all animals used in the experiments and that in all cases the same depth of anesthesia was achieved with this dose. However, this situation apparently is not too significant because cerebral cortex is depressed during urethane anesthesia of moderate depth, whereas the centers regulating the active processes responsible for the compensation of

changes in cerebral blood circulation are thought to lie in the subcortical formations.

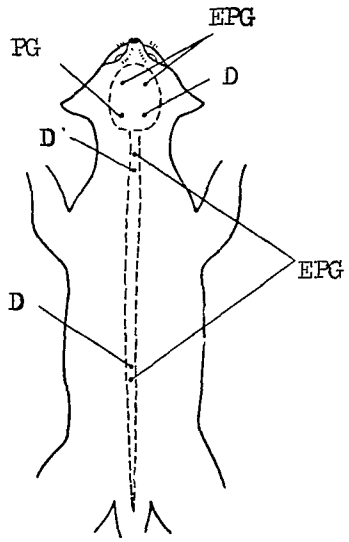

Figure 21. Schematic representation of the arrangement of sensors under conditions of an acute experiment in animals. EPG: electroplethysmogram; D: pressure sensor; PG: polarographic sensor for recording oxygen tension.

To record the intracranial and spinal EPG, the electrodes were introduced bitemporally into the cranial cavity 1.5-2.0 cm away from the median line and into the first cervical and third lumbar vertebrae. The design of the electrodes is shown in figure 22. In carrying out our investigations, on representatives of various classes of vertebrates we made an effort to retain a proportionality between the perimeter of the cranium in its maximum cross section and the diameter of the electrodes. Therefore, in the experiments on frogs and turtles we used electrodes with a case diameter of 1 mm, while for birds and rats we used electrodes with a case diameter of 3 mm. For cats and rabbits, the diameter was 5 mm and for dogs it was 6 mm.

As pointed out above, the values of the electrical parameters between the electrodes placed bitemporally in experiments on various large animals (cats and dogs) were close. After processing the results of 20 measurements, we found that the resistance between the electrodes at a frequency of 35 kHz was 720 ± 216 ohms, while the capacitance was 950 ± 380 mmf. Since we retained a proportionality between the diameter of the electrodes and the internal perimeter of the cranial cavity on the plane where the electrodes were situated, even in the experiments on small laboratory animals the numerical values of electrical conductivity between the electrodes were close to those mentioned above, exceeding them by 15-25 percent. /58

When the electrodes were introduced into the first cervical vertebrae and sacrum, the impedance between them, as determined from 16 measurements, was to 1450 ± 520 ohms, while the capacitance was to 1500 ± 800 mmf.

In a few experiments we observed that the values of electrical parameters between the electrodes were outside these limits. This happened either when

the dura mater was damaged while the animal was being prepared for the experiment or when one of the electrodes was placed over a large blood vessel or when some other mistake was made during the preparation of the animal.

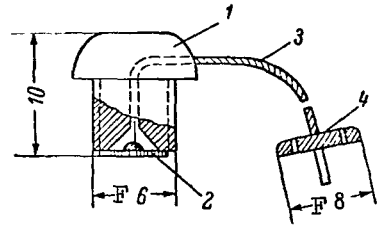

Figure 22. Design of electrodes for recording the intracranial EPG in animals under conditions of acute and chronic experiments. 1. plexiglass case; 2. contact plate; 3. lead wire; 4. reinforcing disk on the skin (for chronic experiments).

As we indicated above, the values of the electrical parameters between the electrodes depend on the frequency used to record the EPGs. As the frequency is increased, the impedance and capacitance decrease, and when it is decreased, they increase.

Intracranial and intravascular pressure sensors were used together with electrodes for recording EPGs in some of the experiments on cats and dogs. The dura mater was removed at the place where the pressure sensor was introduced into the cranial cavity while the interior of the sensor was filled with physiological solution. To measure the intravascular pressures, the sensors were connected to the blood vessels by means of polyethylene cannulas.

A total of 106 dogs, 223 cats, 56 rabbits and 230 rats were used in the series of acute experiments whose results are considered in the present monograph. In the experiments on the other species of animals (pigeons, chickens, turtles, lizards and frogs), only 8 to 12 animals of each type were used because the problem in this case was one of limited interest.

Eight to 25 animals were used in each individual series of experiments depending on the accuracy and reproducibility of the results.

For the chronic experiments, the operations of implanting the electrodes /59
shown in figure 23 were performed on the animals (dogs and cats) under ascetic conditions. The incision was made along the median line of the cranium up to the second cervical vertebra; the edges of the skin wound were kept far apart by hooks. A longitudinal incision of the musculus temparalis was made in the region of the parietal bone, the edges of the muscle were separated by hooks. A hole with a diameter of 5 mm (for cats) and 6 mm (for dogs) was trepanned 1-2 cm from the median line. An identical operation was carried out on the other side of the cranium. To implant the cervical electrode, an incision was made along the median line of the neck muscles. The muscles were scraped from

the first and second vertebrae using a raspatory and were separated by hooks. Trepanation was carried out in the arcus posteriar of the first cervical vertebra and the electrode was introduced. The dura mater was not damaged during trepanation of the hole in the cranium and in the vertebrae. The skin and the subcutaneous tissue structure were incised in the region of the back from the projection of first to the projection of the sixth lumbar vertebrae for implantation of the vertebral electrode. The musculi longissimi dorsi were incised on the right and left of the spinous processes of the second and third lumbar vertebrae, scraped from the vertebrae and pulled back with hooks. An opening was then trepaned in the body of the third lumbar vertebra and the electrode was screwed into it. The wound was sutured layer by layer. The wires from all the electrodes were sutured into the skin wound 0.5 to 1 cm apart between the front oparietal suture and the inion. This is the best place from the standpoint of protecting the wires from damage by the animal. If there was no suppuration, the sutures were removed after 7 to 10 days. The animals were not used until 3 to 4 days after the operation. They were observed for a period of 1 to 3 months, after which time the airtightness of the cranium at the point of electrode implantation was verified in a special acute experiment.

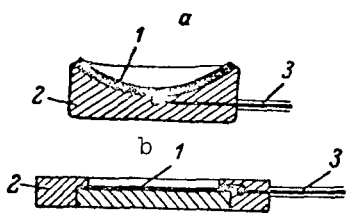

Figure 23. Design of electrodes for recording the intracranial EPG in man when electrodes are positioned as shown in figure 8. a. orbital electrodes; b. occipital electrode. 1. contact plate (silver); 2. plexiglass case; 3. lead wire.

This method was used to operate on 18 dogs and 7 cats. Of these, 8 dogs and 4 cats had electrodes implanted for recording the intracranial and spinal EPGs. Seven dogs and 3 cats had only one pair of electrodes implanted for recording the intracranial EPG, while 3 dogs also had sensors implanted for recording the intracranial pressure together with electrodes for recording the intracranial EPG. The values of the electrical parameters between the electrodes implanted in the cranial cavity and the spine were close to those obtained during acute experiments on animals. However, in the post-operative period and particularly in the first few days after the operation, the impedance between the electrodes increased slightly while the capacitance decreased, appparently the result of regeneration in the region of the electrodes. Stabilization of the values of electrical conductance and capacitance near the electrodes took place at the end of the 2nd or the beginning of the 3rd week after the operation. Six to 10 individual experiments were carried out on each of the operated animals at 1 to 5 day intervals. /60

When intracranial EPGs were recorded in humans, electrodes were placed on both eyes and close to the projection of the foramen magnum. The design of these electrodes is shown in figure 23. In some of the experiments, electrodes were positioned in a different manner: one on the forehead, the other near the mastoid process. The skin around the occiput was defatted and 2 to 3 layers of gauze soaked in a 5 percent salt solution were placed between the skin and the electrode. A total of 35 healthy men and woman aged 20 to 40 years were investigated. Eight were investigated during transverse accelerations on a centrifuge.

Figure 24. Lateral X-ray photograph of a patient's cranium with implanted electrodes.

When the electrodes were placed on the skin of the head, the average value /61
of the impedance between electrodes was 300 ± 120 ohms while that of the capacitance was 1400 ± 550 mmf.

In observations on healthy subjects respiratory movements and EKG were recorded together with the intracranial EPG.

Intracranial EPGs were recorded in 6 patients in the Burden Neurological Institute (Bristol). Approximately 100 electrodes were implanted deep in the frontal lobes. The electrodes were made of gold wire 150 μ in diameter. The insulation at the ends of the wires was removed to a distance 2-3 mm. A few of the electrodes were introduced symmetrically to the right and left subdurally. The lateral X-ray photograph of the cranium of a patient with these electrodes is shown in figure 24.

In patients with implanted electrodes, intracranial EPGs were recorded together with EKGs, respiration, dynamics of the cardiac rate, EEGs and oxygen tension in several regions of the brain.

Processing The Experimental Data

In concluding our discussion of the problems connected with the technique of the investigations, we shall consider several characteristics of the processing of the experimental data obtained by intracranial EPG.

As we pointed out above, quantitative evaluation of blood volume changes in the cranial cavity, which in principle can be made using the diagram shown in figure 6, is difficult to carry out in practice due to errors inherent in the present level of electroplethysmography development. These errors are caused by the uneven distribution of the electrical field in the cranial cavity. We shall therefore, limit ourselves to a qualitative evaluation of the information obtained by intracranial EPG.

In order to permit comparison of the data obtained in experiments on different animals, the changes in electrical conductance reflected in the intracranial EPG curve were expressed in relative units. In some cases this was done by measuring the mean value of electrical conductance between electrodes at the beginning of the experiment and by calibration of the curves during the experiment by switching a constant one-ohm resistance into the circuit of the test object. The calibration signal was used to evaluate changes in the level of the intracranial EPG in ohms. Then, by comparing this quantity with the mean value of the electrical conductance measured at the beginning of the experiment the relative fluctuations in electrical conductance between the electrodes were calculated.

In other cases changes in the parameters of the EPG curves were evaluated /62
by calculating the relative change in a particular index as compared with the initial background signal. For example, the dynamics of the pulse and respiratory waves of the intracranial EPG during the action of gravitational stresses or other factors may be conveniently evaluated in relation to the initial values of these waves. The same method should also be used to evaluate the parameters of the EPG curves obtained by electrodes introduced into the spinal cavity.

The form of the periodic fluctuations in the intracranial EPG--pulse and respiratory waves--is also rather informative along with the value of the amplitude. This is likewise true of the periodic fluctuations in the cerebral blood pressure and in CSF pressure. The form of the pulse waves of the intracranial EPG and fluctuations in blood and CSF pressures were evaluated by determining their spectral composition and by comparing the amplitudes of the higher harmonics with that of the first harmonic. The coefficients of the harmonics were calculated with Simpson's rule, using 18 ordinates. This method of evaluating the form of the EPG pulse waves and intracranial and arterial blood pressures is interesting because the resulting data can be used later for analog simulation of the different individual elements in the cerebral circulatory system.

We sometimes used other methods of evaluating the form of periodic EPG fluctuations in the calculation of the time intervals of the different phases of the curve: time of rise, time of fall, etc. One of these methods of pulse waves on the intracranial EPG is described by Wein and Ronkin (1962).

Section 4. Methods Of Investigating The Intracranial Circulatory System During Increased Gravity

The characteristics of the compensation of the periodic and nonperiodic changes in the blood volume of the cranial cavity during increased gravity were studied on two experimental stands. Longitudinal accelerations of 0.2 to 1 G were produced by changing the position of the animal's body in the vertical plane using a rotating table. The angle of rotation of the table had fixed positions corresponding to accelerations of 0.2, 0.3, 0.4, 0.5, 0.6, 0.8 and 1.0 G. The period of time during which the animal was placed in the required position ranged from 0.2 to 0.4 sec. Experiments on the rotating table made it possible to record several physiological parameters simultaneously using an apparatus the block diagram of which is shown in figure 20.

Longitudinal accelerations over 1 G and transverse accelerations up to 40 G were produced by means of a centrifuge with an arm of 4.5 meters. For /63
loads of 8-15 G the acceleration of the centrifuge was either 1.2-1.5 G/sec (fast) or 0.5-0.7 G/sec (slow), while the deceleration was 1.0-1.5 G/sec. During the experiments on the centrifuge machine it was possible to record an intracranial EPG intracranial pressure, EKG, and respiratory movements.

Longitudinal accelerations of up to 1 G were produced by rotating the table while the transverse accelerations were produced on the centrifuge. This was done in the case of both humans and animals.

The duration of gravitational stresses did not, as a rule, exceed 15 or 30 sec. In some experiments the action was continued 1, 3, and 5 minutes. Each animal was subjected to several such separate actions in acute and chronic experiments. The time interval between such loads was 2 to 10 minutes depending on the rate at which the initial indices were restored. Observations on humans over a day involved 3 to 5 brief actions of up to 1 G or one action of a higher intensity.

In the present section we could have limited ourselves to listing the stress conditions to which the subjects were exposed, thereby satisfying the problem described in the sections dealing with the experimental technique. However, the behavioral characteristics of the cerebrovascular system during slight gravitational stresses are of great interest not only for space physiology but also from the standpoint of methods used to study the cerebral circulatory system both under normal conditions and in different pathological states.

Observations on the intracranial circulatory processes in an animal at rest do not always yield much information. It is true, of course, that under normal conditions the intracranial circulation is always undergoing rhythmic changes, caused by cardiac activity and respiration, and these rhythmic changes may be considered definite test actions on the system. Analysis of the reaction of the intracranial circulatory system to pulse and respiratory changes in blood flow yields significant information on its function. However, the changes in the intracranial circulatory system caused by cardiac contractions and respiratory movements are small. Hence, they are unsuitable for the study of the intracranial circulatory system reaction and do not provide sufficiently complete information on all the peculiarities of this system. This would require stronger disturbances.

Several methods have been developed during the past 20 years for investigating the intracranial circulatory system. Some of them broaden the possibilities by perfecting the technique of investigations, while others do so by developing new variations of the experiments. The first group includes the now classical method of Hürthle, which uses the difference in the pressures in the central and peripheral segments of the internal carotid artery to obtain information on the reactions of the regional cerebral arteries and of the arteries at the base of the cranium. The first group also includes the Gartner-Wagner method, which is useful in evaluating the state of venous release flow from the cranium. /64

Avrorov (1957) proposed a new method for the contactless measurement of blood pressure differences in arteries at the base of the cranium and of the systemic arterial pressure in animals with the carotid artery drawn into a skin flap, which is a modification of the Hürthle method.

A new modification of the Hürthle method proposed by Usov (1960) consists of measuring the difference in the spinal and subclavian arteries with ligation of the lateral trunks. The first group also includes such methodical approaches as the "chest-head" preparation (Mchedlishvili, 1962), which permits stabilization of the parameters of cardiac action, and this in turn makes it possible to study the reaction of cerebral vessels to various stimulations under isolated conditions. The first group likewise includes the model of a dog's head with isolated circulation proposed by Mikhaylov (1966).

The second group of methods includes the familiar Valsalva, Queckenstodt, Müller, and Stookey tests. The occlusion test is of great interest in this connection. Occlusion of the superior vena cava enabled Mchedlishvili et al. (1962) to discover the specific reactions of the regional cerebral arteries. Investigations involving occlusion of the arterial trunks that supply the brain with blood made it possible to obtain a new data on the role of the mechanoreceptors of the carotid zones in maintaining the normal cerebral blood level (Blinova and Marshak, 1963) and also on the effectiveness of collateral cerebral blood supply.

A variety of chemical and mechanical actions are now used as tests in the study of the cerebral circulatory system.

While studying the effects of longitudinal accelerations on the cerebrovascular system we became convinced that such loads (up to ±1 G) might be a good test for investigating the characteristics of this system under normal conditions. Indeed, such reactions satisfy all the demands made on tests. First, longitudinal accelerations act on specific elements of the intracranial circulatory system. In this connection they correspond to orthostatic tests which have been widely used of late to investigate intracranial circulation. Second, this form of stimulation can be accurately dosed according to three basic indices: intensity, rate of increase, and duration. Thirdly, such reactions are quite "physiological" for most laboratory animals and for man.

We therefore used longitudinal accelerations of 0.2 to 1.0 G, produced by a rotating table, as a test stimulant to study certain special features of the mechanisms of compensation of changes in the blood volume of the cranial cavity.

We investigated other methodology besides longitudinal accelerations, namely, occlusion of the superior vena cava and jugular veins, Hürthle's method, and the Valsalva, Stookey, and Miller tests.

CHAPTER 2. BASIC MECHANISMS OF COMPENSATION OF CHANGES IN THE BLOOD VOLUME OF THE CLOSED CRANIAL CAVITY

Intracranial circulation has special features which distinguish it from /66
blood flow in other parts of the body and organs. To begin with, cerebral blood flow is very intense. Many investigators employing different methods in recent years have shown that the average intensity of cerebral blood flow is 50-60 milliliters a second per 100 grams of brain (Dumke and Dumke, 1941; Kety, 1948; Lassen and Munk, 1955; Lassen et al., 1963; others). Brain tissue is very sensitive to even transient disturbances of circulation because basal metabolism in the brain is of an aerobic nature and, moreover, an oxidizable substrate depot is absent in the brains of higher vertebrates.

Blood flow in brain tissue is distributed unevenly. Sokoloff and Landau (1955) showed that the blood flow is most intense in the cortical, auditory, and visual regions of the cortex, achieving a value of 1800 milliliters a minute per 100 grams of brain.

The density of the capillaries in these regions is 200 to 300 times greater than in the white matter (Polyakov, 1949).

It is reasonable to conclude from the above data that the intensity of cerebral blood flow is 10 times greater than the average level of blood flow in other organs and tissues. The intensity of blood flow in the cerebral cortex, where the volume occupied by the blood vessels is approximately 24 percent of the total tissue volume (Hale and Reed, 1963) while the capillaries occupy 5 to 6 percent of this volume (Isikawa, 1950), exceeds the average intensity of blood flow more than 50-fold. This high intensity of blood flow is characteristic of the brain in a variety of functional states--during sleep and during wakefulness, in a coma, and during mental activity, in many pathological states, and during the action of pharmaceutical agents. It is thus a rather stable quantity (Konradi and Parolla, 1963).

It is difficult to reconcile the same high intensity of cerebral blood /67
flow under different conditions, an indication of its efficient control system, with another feature of the intracranial circulatory system--the limited volume of fluids in the closed cranial cavity. It would seem that this limitation should inhibit the realization of the regulatory processes.

The limited volume of the cranial cavity was at one time the basis for the conception that the blood volume in the closed cranial cavity is invariable--the Monroe-Kelly doctrine. Many well-known physiologists of the past adhered to this doctrine, notably Starling and Sherrington. The Monroe-Kelly doctrine was the object of many discussions which resulted in a cycle of investigations that laid the foundation for the theory of compensation of changes in the blood volume of the closed cranial cavity (Salathe, 1876; Mosso, 1881; Geigel, 1905; others).

Investigations in this direction, which have continued until the present day, have shown convincingly that the Monroe-Kelly doctrine is untenable.

According to the modern concepts of the physiology of intracranial circulation, there are two possible methods for the compensation of changes in the blood volume of the closed cranial cavity. These are based on its structural characteristics. The first possibility is that the compensation of changes in the blood volume of individual regions of the cerebrovascular system and meninges results from the redistribution of the arterial and venous blood or from the related changes in the blood volume of the functioning and nonfunctioning parts of the region. The second possibility is that the compensation of changes in the cerebral blood volume as a whole is due to the movement of the CSF between the CSF spaces of the brain and spinal cord.

Thus, the possible mechanisms for the compensation of changes in the cerebral blood volume may be represented in a simplified manner by the diagram shown in figure 25. The cerebrovascular system is represented by two separate volumes corresponding to the arterial V_a and venous V_v systems whose interaction provides the first possibility for the compensation of changes in the cerebral blood volume. This diagram also provides for a communication between the cranial and spinal cavities through a hole of limited diameter thanks to which the compensatory movements of the CSF are possible.

The cerebral arterial and venous systems and the spinal cavity are somewhat elastic. The cranial cavity also has a rather small elasticity, which is less than that of the spinal cavity. Apparently the blood flow in the cerebral vessels takes place because the pressure levels in the arterial and venous /68
systems are maintained by external forces--by the systemic arterial and venous pressures. The diagram takes into account the possible effect produced by the blood volume level in the broad system of venous sinuses of the spinal cord V_s on the movement of the CSF between the cranial and spinal cavities, i.e., its effect on one of the mechanisms for the compensation of changes in the volume of cranial blood. The arterial system of the spinal cord is not shown because it is much less developed than the cerebral arteries.

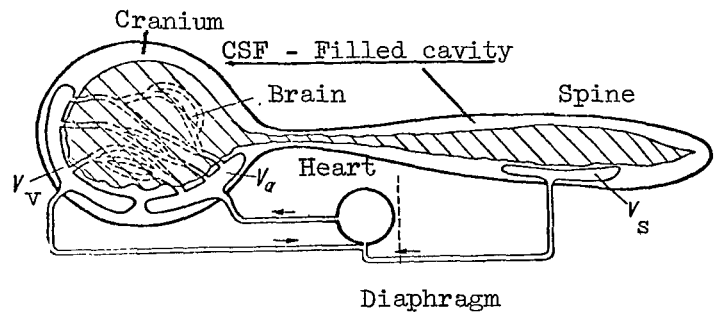

Figure 25. A simplified diagram showing the hydrostatic relations which ensure compensation of the cranial cavity blood volume. V_a and V_v are the spaces occupied by the arterial and venous cerebral systems; V_s is the space occupied by the venous plexuses and sinuses of the spine. Arrows show the direction of blood flow.

How well does this diagram reflect the true picture of the hydrodynamic relations, in the closed cranial cavity? What are the capabilities of the two mechanisms of compensation of changes in the blood volume of the cranial cavity and what is the relationship between them? Are these the only possibilities for compensation? The purpose of this chapter is to consider these questions.

Section 1. Compensation Of Changes In The Blood Volume Of The Closed Cranial Cavity Due To Interaction Between The Arterial and Venous Systems Of The Brain

We may conclude from the diagram shown in figure 25 that the necessary condition for the compensation of changes in the blood volume of the cranial cavity due to interaction between the arterial and venous systems is the direct mechanical connection between the spaces occupied by the arterial and venous systems. This connection may be ensured by the movement of the CSF in the cranial cavity occurring as a result of small displacements in the cranial mass. Many investigations with simultaneous recording of arterial and venous blood pressures in the cranial cavity have shown that this connection between the two /69 systems does in fact exist and that the CSF serves as the transmitting medium in the closed cranial cavity. A detailed analysis of the experimental data from the 1920s and 1930s showing this connection was made by Sepp (1928) and the experimental data published in recent years confirmed it.

Schroeder (1953) again verified the possibility of transmission of arterial pressure to the veins by recording simultaneously the pressure in the internal carotid artery, subarachnoid space, and jugular vein. He used electromanometers because he assumed that errors may have occurred in the previous investigations due to the use of water manometers. He became convinced that arterial pressure can be transmitted to the veins. The relationship between pressures in the cerebral arterial and venous systems is the basic condition for the compensation of changes in the cerebral blood volume, but it does not by itself show the presence of such compensation. Direct proof of its existence is provided by the facts on the nature of blood release from the cranium. Berthold (1869) was the first to show that blood release from the cranium has a pulsating nature. Later the pulsating release of venous blood was recorded by Keller (1939) and by Kedrov and Naumenko (1954) using a more refined method. What is the origin of this pulsation? Pulse changes in the blood flow may reach the venous system by traveling along the vascular bed or they may result from the compensation of pulse increases in the volume of arterial blood in the cranial cavity. Data obtained by direct observation of the cerebral capillaries (Klosovskiy, 1951) have shown that their blood flow does not undergo any pulsating changes. Consequently, it is most probable that the pulsating outflow of blood from the cranium is due precisely to the above mechanism of compensation of changes in the blood volume of arterial vessels in the cranial cavity.

Thus, an increase in the volume of arterial blood in the cranial cavity may be compensated by a decrease in the volume of blood in the venous system accompanied by an intensified outflow of venous blood from the cranium. The rate of such compensation must be high. This follows from the fact that the

cross section of venous pathways which transport blood from the cranium is quite large.

In order to determine the dynamic nature of compensation of changes in volume of arterial blood, we simultaneously recorded pulse fluctuations in the venous and CSF pressures with a subsequent harmonic analysis of the resulting curves (fig. 26). We found that the spectral composition of the pulse fluctuations in the CSF and venous pressures is approximately the same, but the high-frequency harmonics, beginning with the fourth, are less on the venous pulse curve in comparison with the pulse of the CSF. This means that the limitations in the rate of compensation are noticeable only at frequencies 4 to 5 times greater than the cardiac rhythm. /70

It is not to be excluded that the limitation in the rate of compensation is due to the properties of the walls of the venous vessels which transmit the CSF pressure to the venous blood after some delay, rather than to the impossibility of such a rapid release of blood from the cranium. In any case, however, this means that the limitations in the rate of compensation due to venous release will be manifested during rapid changes in the blood volume.

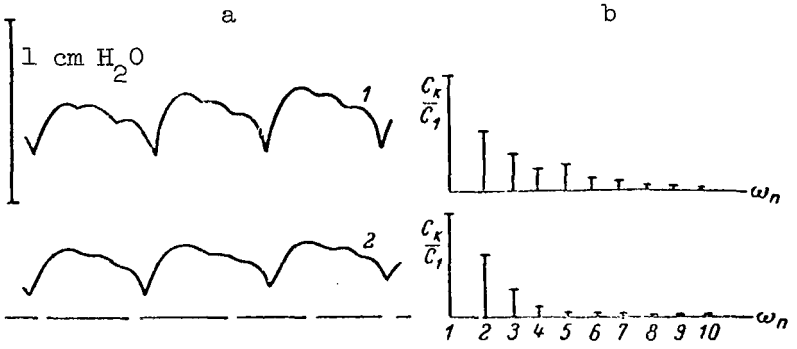

Figure 26. Pulse waves (a) of intracranial pressure (1) and of pressure in the longitudinal sinus (2) and the harmonic composition of these fluctuations (b). ω_n - number of the harmonic; C_k/C_1 - ratio of the amplitude of the k-th harmonic to the amplitude of the first one.
Time marker - 0.5 sec.

Thus, the above data indicate that there are no significant time limitations in the compensation of an increase in the arterial volume due to the intensified outflow of venous blood from the cranium.

Let us now consider the volume possibilities of compensating dilatation of the arterial vessels due to venous release. These possibilities are

presumably small. The limitation in the volume possibilities of such compensation follows from the fact that a decrease in the volume of the cranial veins leads to an increase in the hydrodynamic resistance of the cerebrovascular system as a whole despite the dilatation of the arteries. This proposition was proved theoretically by Geigel (1905).

The idea behind Geigel's calculations is as follows. The total hydrodynamic resistance of the cerebrovascular system W may be expressed as the sum of the resistance of the arterial W_a and venous W_v systems which in turn are equal to /71

$$W_a = \frac{K_a l_a}{q_a^n} \text{ and } W_v = \frac{K_v l_v}{q_v^\nu}, \quad (1)$$

where l_a and l_v, q_a and q_v are the equivalent cross section and length of the arterial and venous systems; K_a, K_v, n and ν are coefficients reflecting the properties of the vascular wall of the blood, with n and ν less than 1.

We assume that the total cerebral blood volume is constant

$$V_k = q_a l_a + q_v l_v. \quad (2)$$

This condition means that the arterial blood volume of the cranial cavity can be changed only by the mechanism of compensation under study--as a result of the redistribution of the volumes occupied by the arterial and venous systems. In this case the volume of the CSF in the cranial cavity remains constant.

It follows from equations (1) and (2) that the total hydrodynamic resistance to the blood flow in the cranial cavity is

$$W = \frac{K_a l_a}{q_a^n} + \frac{K_v l_v^{\nu+1}}{(V_k - q_a l_a)^\nu}. \quad (3)$$

Let us find the conditions in which W has minimum value. Assuming that $\frac{dW}{dq_a} = 0$, and finding that $\frac{d^2W}{dq_a^2} > 0$, it turns out that W acquires the minimum value when

$$W_a = W_v \frac{\nu l_a q_a}{n l_v q_v}. \quad (4)$$

Expression (4) shows the relationship between the total hydrodynamic resistance of the cerebrovascular system and the space occupied by its arterial system. This relationship is shown graphically in figure 27.

The curve in figure 27 will be displaced parallel to the axis of the abscissas depending on the volume of the CSF in the cranial cavity.

According to Geigel, under normal conditions W has a value close to the minimum, i.e., the ratio of the equivalent lengths and cross sections of the arterial and venous systems is determined by expression (4), which appears to us to be quite plausible. Therefore, a redistribution between the arterial and venous blood volumes in the cranial cavity occurring during various processes in the cerebrovascular system as a result of an increase or decrease in the volume of arterial blood will lead to an increase in W and consequently to a deterioration in the cerebral blood flow.

Having dwelt on this stage of Geigel's calculations, we can agree with the /72
validity of his conclusion in spite of the fact that it has been criticized by Sepp (1928) and other investigators, because all the objections mentioned in the literature pertained to the subsequent arguments of Geigel, which were oversimplified from our standpoint.

The relationship between the total hydrodynamic resistance of the cerebral vessels and the spaces occupied by the arterial and venous systems shows that there is a volume limitation to this type of compensation. Indeed, a change in relationship between the arterial and venous systems results in deterioration of the cerebral circulation and the concept of "compensation" thus loses its meaning.

On the basis of the rate and volumetric characteristics of this type of compensation of changes in the cerebral blood volume under study, it is fair to conclude that such compensation is effective when there are sharp changes in the arterial blood volume of the cranial cavity occurring in short time periods during which the dynamic resistance to blood flow increases insignificantly. Upon a deterioration in the conditions for the outflow of venous blood from the cranial cavity, the efficiency of this form of compensation drops.

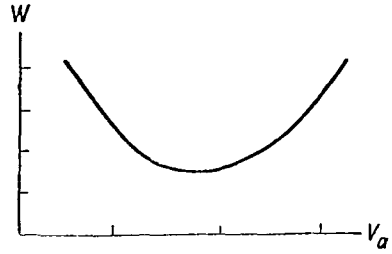

Figure 27. Hydrodynamic resistance of the cerebrovascular system (W) as a function of the volume occupied by the arterial system (V_a). This curve is a graphic representation of the relationship expressed by equation (4).

It is obvious that change in the relationship between the volumes of the arterial and venous system, in turn, leads to change in CSF pressure. This creates the conditions for the second mechanism of compensation of changes in the cerebral blood volume as a result of the movement of CSF from the cranial cavity into the spinal cavity and back when there are changes in the volume of the cerebrovascular system. This will be considered below.

Section 2. Compensation Of Changes In The Cerebral Blood Volume Produced By The Movement of CSF Between The Cranial And Spinal Cavities

The idea of such compensation of changes in the volume of cranial blood was advanced in the middle of the last century by Richet (1848), who assumed that a definite quantity of subarachnoid fluid "flows" from the cranial cavity into the spinal cavity and back. The author concluded that there is an "antagonism" between the intracranial and spinal cavities in regard to the volume occupied by the CSF. /73

This mechanism of compensation assumes above all the possibility of more-or-less free communication between the CSF spaces of the cranial cavity and of the spine.[1]

To demonstrate this possibility, we shall examine the results of investigations on the movement of CSF as a result of secretory pressure, conducted with the aid of dyes and later with the aid of radioactive isotopes. Although these investigations showed that various dyes and radioactive isotopes shift from the cranial cavity into the spinal cavity and back, the resulting ideas on the movement of CSF under the influence of secretory pressure are rather contradictory, as we have pointed out above (page 4).

Of the many investigations devoted to the study of CSF movement, mention should be made of the work of Vasilevskiy and Naumenko (1959), who recorded the spreading of radioactive isotopes introduced into the ventricles and confirmed that CSF in a rigidly fixed animal moves in the caudal direction. They also established the fact that its linear flow rate along the spinal cavity averages 0.299 mm/min. We agree with these data because the measurements of Vasilevskiy and Naumenko were performed with advanced techniques which took into account errors introduced by the recording equipment.

The movement of the CSF is also confirmed by the recently published investigations of Bradbury et al. (1964), who showed that within two hours a dye introduced into the subarachnoid space of a rabbit spreads to the subspial spaces of the spinal cord to a distance of 3-4 cm. Thus, the facts indicate that there is communication between the cranial cavities and the spinal cavities. The diagram of the mechanism for the stationary movement of the CSF according to recent physiological and anatomic data is shown in figure 28.

A mass of data indicate that under normal conditions the forces necessary for compensatory movement of the CSF between the cranial and spinal cavities arise. This is confirmed by data on the rapid change in the correlations of pressures in the large occipital and CSF cisterns when the position of the body

[1] Here and in the future we shall use the expressions "cranial cavity" and "spinal cavity" when discussing the movement of the CSF. We take them to mean subpial spaces and cisterns of the brain and of the spinal cord filled with CSF.

is changed in the vertical plane and during various movements (Sieven, 1897; Meyerson and Loman, 1932; Dumarco and Rimini, 1947; Mangold, 1954; Fridman, 1957). /74

Direct proof of the existence of compensatory movements of the CSF between the cerebral and spinal cavities was obtained when intracranial and spinal EPGs were recorded simultaneously in animals (dogs and cats) in chronic experiments (Moskalenko and Naumenko, 1959a). These experiments showed that changes in the levels of the intracranial and spinal EPGs in response to various actions are in the opposite direction, i.e., when the blood volume of one of the cavities increases, the blood volume of the other cavity decreases, and vice versa (table 3). This shows the existence of conjugate changes in the volume of the CSF in cranial and spinal cavities. As is evident from table 3, the greatest movements /75 of the CSF are recorded when the head is lifted, lowered or turned, and when the position of the body is changed.

The CSF also moves during the lifting of paws, yawning, stretching, etc.

Marked movements of the CSF occur when the position of the animal in the vertical plane is changed. This happens under the influence of the longitudinal gravitational acceleration by earth's gravity.

The extent of CSF movement under the influence of gravity when the head is lited and lowered depends to a large degree on the position of the animal's body. If the animal is horizontal (standing or lying), the amount of CSF that moves when the head is raised is 1.5-2 times greater than when the animal is sitting /76 (table 3). The movements of the CSF in the reverse direction occur for several seconds after the body or head of the animal returns to its initial position.

The conjugate nature of the changes in CSF pressure and its compensatory movements is indicated by data on the dynamics of the pressure of cranial cavity blood when the abdomen is squeezed (Stookey's test). We obtained this information by simultaneously recording the intracranial EPG and pressure in experiments on animals (fig. 29).

It is generally known that in Stookey's test, change in blood pressure of vertebral venous plexuses impedes the release of blood from the spine, resulting in an elevation of CSF pressure. This elevation of pressure is transmitted to the cranial cavity in accordance with hydrostatic laws. The decrease in total blood volume of the cranial cavity accompanied by an increase in the intracranial pressure when the abdomen is squeezed (fig. 29) shows that such an action results in the CSF moving from the spinal cavity into the cranial cavity and this movement, as we can see in figure 29, does not take place instantaneously but rather for several seconds.

All these facts quite clearly show that changes in the blood volume of the cranial cavity are compensated by the movement of CSF between the cranial and spinal cavities.

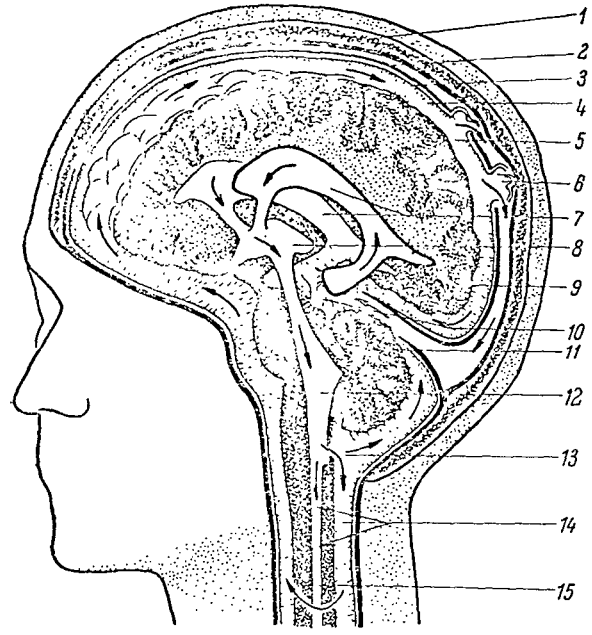

Figure 28. Schematic representation of CSF pathways in the subarachnoid space and in the cervical region of the spine (from Strand, 1965). 1. cranium; 2. dura mater; 3. subdural space; 4. arachnoid membrane; 5. subarachnoid space; 6. evagination of the arachnoid membrane; 7. lateral ventricles; 8. third ventricle; 9. pia mater; 10. choroid plexuses; 11. cerebellum; 12. fourth ventricle; 13. union of the fourth ventricle and the subarachnoid space; 14. CSF; 15. central spinal canal.

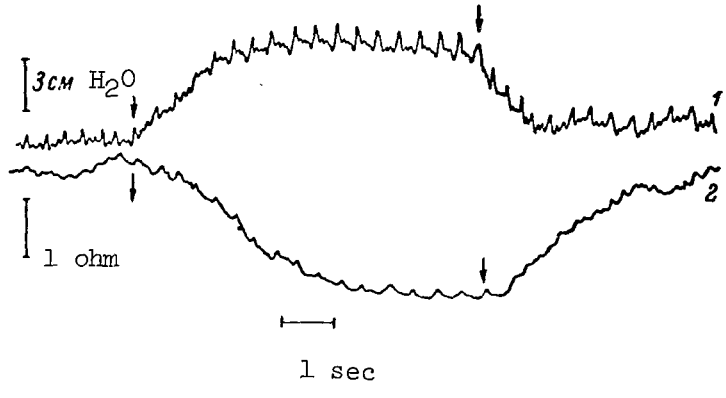

Figure 29. Change in intracranial pressure (1) and blood volume of the cranial cavity (2) when the abdomen of a cat is squeezed. Acute experiment. Arrows indicate the beginning and end of the stimulation.

TABLE 3. CHANGES IN THE BLOOD VOLUME OF CRANIAL AND SPINAL CAVITIES DURING DIFFERENT MOVEMENTS OF THE ANIMAL (RESULTS OF A CHRONIC EXPERIMENT)

Position of the animal's body	Nature of the movement	Electrical resistance of the cranio-spinal cavity (in relative units)			The electrical resistance of the spinal cord (in arbitrary units)		
		before movement	after movement	after return to the initial position	before movement	after movement	after return to the initial position
			Cat (weight 3 kg)				
animal	lifting of the head	33	38	33.5	17	11	18
	rotation of the head	30	32	30	19	18	19.5
	lifting of the forward part of the body	33	35	32	18	22	19
	transition to a sitting position	34	23	-	19	25	-
the animal sits	lifting of the head	20	22.5	20.5	25	24	25
	lowering of the head	21	20	21	24	26	25
	Queckenstedt's test	36	41.5	35	24	18	23
			Dog (weight 8 kg)				
the animal stands	lifting of the head	18	24	19	21	17	22
	lowering of the head	19	16	18	19	22	-

Once we are aware of the existence of compensation movements of CSF, it is easy to identify the source of the conflicts in some of the views on the direction of the stationary CSF flow under the influence of secretory pressure. /77
Indeed, the final results of investigations with the use of dyes and radioactive isotopes are determined not only by the directed movement of the CSF under the influence of secretory pressure, since the rate of this movement is rather low, but also by the effect of various associated factors particularly by the movements of the object under study. However, in some series of experiments when the animal was secured quite firmly, for example in the experiments of Vasilevskiy and Naumenko (1959), only the stationary flow of the CSF under the influence of secretory pressure was recorded, although in these experiments errors were introduced by the pulse and respiratory waves.

Consequently, the results of many experiments involving the use of dyes and radioactive isotopes, in spite of their outward inconsistency, not only demonstrate a direct communication between the CSF spaces of the cranial and spinal cavities but also indicate that there are compensatory movements of the CSF between the cranial and spinal cavities.

Let us now examine the possible speed of this type of compensation. According to the diagrams shown in figures 25 and 28, the cranial and spinal cavities communicate with each other through an opening of limited size. This probably limits the rate of compensation of the changes in the blood volume of the cranial cavity due to the outflow of the CSF.

In order to determine the effect of such a limitation on the rate of compensation of changes in the volume of the cranial cavity, let us consider the interaction of the blood volumes and of the CSF in the closed cranial cavity by slightly changing the diagram shown in figure 25. That is, let us assume that change in blood pressure P_{bl} in the elastic vascular system has no limitations on velocity and that the release of the CSF under pressure P_l from the cranial cavity may take place through an opening of limited cross section into the spinal cavity, which has a certain amount of resilience.

From the data on the relationship between the extent of vascular wall distension and the distending force (Savitskiy, 1956; Read, 1957; others) it is reasonable to assume that slight blood pressure changes $d\Delta P_{bl}$ inside the elastic membrane are caused by changes in the blood volume $d\Delta V_{bl}$ by a linear relationship

$$d(\Delta P_{bl} - \Delta P_{csf}) = L \frac{d\Delta V_{bl}}{V_{bl}}, \qquad (5)$$

where L is the quantity which characterizes the elastic properties of the vascular wall, and V_{bl} is the value of the blood volume in the cranial cavity at a given moment.[1]

[1]Footnote on the next page.

The condition for a constant volume of fluids[1] in the cranial cavity may be /78 expressed by the following relationship

$$d(\Delta V_{bl} + \Delta V_{csf}) = 0, \tag{6}$$

where ΔV_{csf} is the change in the cerebral CSF volume. The limitation on the volumetric flow rate in the region where cranial and spinal cavities meet can be determined by the following formula:

$$\frac{d\Delta V_{csf}}{dt} = \frac{A}{\eta} \Delta P_{csf}, \tag{7}$$

which is analogous to Poiseuille's formula where η is the coefficient of viscosity of the overflowing fluid and A is some constant characterizing geometry of the opening. According to Poiseuille's formulas, A is expressed in terms of the radius and length of the release tube. Changes in CSF pressure and volume in the spinal cavity are linked by the following equations:

$$\frac{d\Delta V_{csf}}{dt} + \frac{A}{\eta \alpha_{csf}} \Delta V_{csf} = -\frac{A}{\eta} \Delta P_{csf}. \tag{8}$$

Solving equations (5), (6) and (7) for ΔV_{bl} and ΔP_{bl}, we obtain

$$\Delta V_{bl} = \alpha\beta e^{-\beta t} \int_0^t \Delta P_{bl}(t)\, e^{\beta\tau} d\tau, \tag{9}$$

$$\Delta P_{csf} = \frac{1}{\alpha}\left[\Delta P_{bl}(t) - \beta e^{-\beta_1 t} \int_{-\infty}^{t} \Delta P_{bl}(t)\, e^{\beta_1 \tau} d\tau\right], \tag{10}$$

where

$$\beta = \frac{\eta A}{\alpha}, \quad \alpha = \frac{V_{bl}}{L} \quad \text{and} \quad \beta_1 = \beta + \frac{A}{\eta \alpha_{csf}}.$$

(See preceding page)

Here and in the future discussions we shall use the terms "blood pressure" (P_{bl}) and the "blood volume" (V_{bl}) in cases when the laws under consideration are equally valid for both the arterial and venous systems. However, when comparing the effects caused by changes of pressure in this system, one must allow for the difference in the mean pressures of the arterial and venous systems and the difference in the transfer coefficients of these pressures to the CSF.

1 This condition means that the cranial cavity cannot be stretched and its blood volume can be compensated only by the outflow of the CSF.

Equations (8) and (9) characterize in a general form the volumetric rate of compensation of changes in the cerebral blood volume due to release of the CSF.

For a specific case when there is a sudden change of pressure in the intracranial circulatory system which is equivalent to an equally rapid change in the elasticity of the vascular system during an active reaction, the solution of equations (9) and (10) for changes in the cerebral blood volume ΔV_{bl} and intracranial pressure ΔP_{bl} will be expressed in the form of equation (11) or in the form of graphs shown in figure 30. /79

$$\left.\begin{aligned} \Delta V_{bl} &= \alpha \Delta P_{bl}(1 - e^{-\beta t}), \\ \Delta P_{csf} &= \frac{1}{\alpha} \Delta P_{bl}\left[1 - \frac{\beta}{\beta_1}(1 - e^{-\beta_1 t})\right] \end{aligned}\right\} \qquad (11)$$

The correctness of expression (11) can be verified experimentally because it is possible to achieve by a final jump a sufficiently rapid change in the cerebral blood pressure by changing the position of the animal in the vertical plane by some angle θ. Sin θ is proportional to the magnitude of the jump ΔP_{bl} because the main blood vessels which supply the cranium and which transport blood from the cranium are almost parallel to the longitudinal axis of the body. When the head is lowered (which corresponds to a negative gravitational stress), the changes in blood volume of the cranial cavity can be compensated only by the release of CSF. This is so because in this case the release of the blood from the cranium is inhibited. There is a substantial increase in the venous pressure of the cerebral vessels and the route of compensation of the cerebral blood volume considered in the preceding section is blocked.

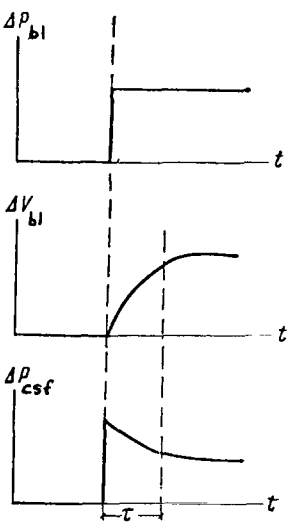

Figure 30. Change in the cerebral blood volume (ΔV_{bl}) and intracranial pressure (ΔP_{bl}) after an abrupt change in blood pressure (ΔP_{bl}) (results of calculations).

The fact is that under normal conditions pressure in the venous cerebral system is low. According to Fleisch (1927), pressure in the jugular veins may have a value up to 0.5 mm Hg, i.e., it is lower than that of other venous trunks of the same caliber. Therefore, the change in the height of the blood column by several centimeters during longitudinal gravitational stresses will produce a substantial change in the cranial venous pressure and will have practically no effect on the arterial pressure. This is confirmed by the investigations of Gauer and Henry (1964), who established that with negative accelerations of 10 G the venous pressure in the cranium rises to 200 mm Hg and becomes close to arterial pressure. During negative acclerations of up to 1 G, the venous pressure in the cranium, according to our data, increases more than 3-fold, while the arterial pressure increases by several percent (table 4). Thus, changes in the cerebral blood volume during negative gravitational stresses affect primarily the venous system. This fact was recently confirmed by the investigations of Benua et al. (1966). With fairly low values of θ (usually $\sin\theta<0.5$) lying below the threshold of active cerebrovascular reactions, the cerebral blood volume changes according to a law close to the theoretical (fig. 31). We have also observed an exponential relationship in the cerebral blood volume when the position of the body is rapidly changed in the vertical plane during experiments on fresh carcasses of animals previously injected with heparin (fig. 32). Here, unlike the case of live animals, the exponential relationship persists, up to the value $\sin\theta=1$. Recording changes in the intracranial pressure simultaneously with an EPG (fig. 31) has shown that at the beginning of the action, intracranial pressure increases sharply but then decreases somewhat following a law which is close to exponential, i.e., the nature of its changes corresponds to the theoretical curve described by equation (11) and presented in figure 30.

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The results of the above experiments show that the rate of compensation of changes in the blood volume of the craniocerebral cavity due to the release of the CSF into the spinal cavity is quite limited because of limited transmission capacity in the region of the foramen magnum. When changes in blood pressure are abrupt, blood volume changes exponentially and the time constant of the exponent τ serves as an indicator of this limitation and characterizes the volumetric rate of the compensatory movements of the CSF.

Table 4. RELATIVE CHANGES IN THE ARTERIAL AND VENOUS BLOOD PRESSURES OF THE CEREBROVASCULAR SYSTEM IN A CAT DURING NEGATIVE GRAVITATIONAL STRESSES.

Intensity of negative longitudinal load (in G)	Relative change in pressure (percent of normal, mean of 5 experiments)	
	Arterial system	Venous system
0.2	0	23
0.4	0	52
0.6	0	88
0.8	5	110
1.0	12	155

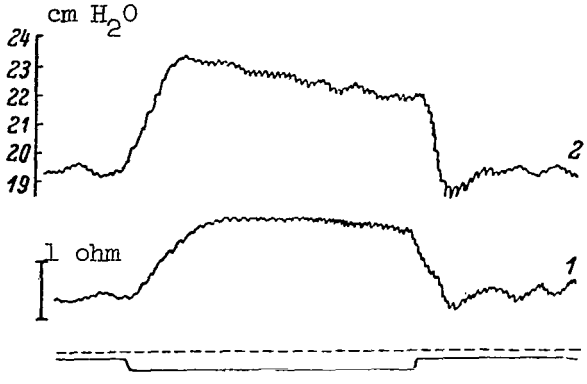

Figure 31. Change in the cerebral blood volume (1) and intracranial pressure (2) of a cat after a sudden change in position of the body from horizontal to vertical with the head down (acceleration of 0.5 G). Acute experiment. Time marker - 1 sec.

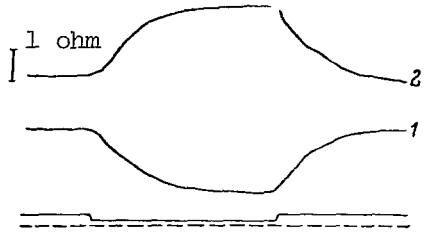

Figure 32. Change in the cerebral blood volume of a fresh cat carcass produced by an abrupt change in the position of the body. 1. rotation of the body with the head up; 2. the same with the head down. Time marker - 1 sec.

Experiments performed by us jointly with A. A. Shurubura and D. I. Pesennikova on four representatives of the vertebrates (amphibians, reptiles, birds and mammals) and observations on man have shown that the exponential law of change in the cranial cavity blood volume during changes of body positions in the vertical plane applies to all these animals and man. Although τ changes within broad limits not only for representatives of a single class or order but also for representatives of the same species of experimental animals, information obtained from many experiments reveals some statistical tendencies in changes in τ.

For example, τ decreases regularly in some vertebrates with the development level of the CNS. In experiments with the same animals, the establishment of a stable level of blood volume is more frequent during positive gravitational stresses than during negative ones.

A similar pattern has been observed in man; τ changes sharply in animals in a preterminal state produced by deep anesthesia (table 5).

It is possible that in the last two cases changes in the rate of compensation of the cranial cavity blood volume are due to changes in the effective cross section of the opening which connects the cranial cavity with the spinal cavity. In the first case it is due to some displacement of the cerebral mass, while in the second case it is due to the developing edema of the brain. /82

Table 5 shows the mean values of τ obtained from analysis of changes in the intracranial EPG level after sudden changes in the position of the body for several forms of animals. By comparing the quantity τ with the time t required for the blood pressure change to reach its maximum value during the process under study, we can evaluate the correlation between the rates of the process compensated and the compensatory movement of the CSF between the cranial and spinal cavities. This correlation will be observed when $\tau<t$.

When $\tau>t$, change in the blood volume of the cerebrovascular system, as follows from equation (9) and (10), will result in major changes in intracranial pressure and in minor changes in the cerebral blood volume compared with changes in these parameters when $\tau<t$. Also, this difference between changes in the intracranial pressure and blood volume will increase as t decreases. The foregoing is confirmed by comparing the amplitudes of the pulse and respiratory changes in intracranial pressure and cranial cavity blood volume (fig. 33). It is easy to see that the ratio of the amplitudes of the pulse waves to the respiratory waves on the intracranial pressure EPG curve is 0.4, while on the intracranial EPG curve it is 0.15. In other words, the pulse fluctuations are more pronounced on the first curve, which is characterized by a high rate of change in pressure, while the slow respiratory waves are more pronounced on the second curve. /83

TABLE 5. MEAN VALUES OF THE TIME CONSTANT τ DURING SUDDEN CHANGES IN THE POSITION OF THE BODY IN SOME ANIMALS AND IN MAN.

Subject	Load in G	number of investigations	time required to achieve a maximum change in the cerebral blood volume (sec).
a cat under urethane anesthesia of moderate depth	+0.4	12	3.6±0.8
	-0.4	10	2.7±0.7
a cat in the preterminal state	-0.4	9	6.4±1.8
frog	-0.4	7	10.5±2.8
turtle		8	8.2±2.2
lizard		12	5.2±1.8
chicken		7	4.3±1.2
pigeon		8	2.8±1.0
cat		10	2.7±0.7
man		6	2.1±0.6

Thus, the factual data confirm the idea expressed above that the volumetric rate of compensation of changes in the cerebral blood volume due to movement of the CSF between the cranial and spinal cavities is limited. The available information is insufficient for quantitative evaluation of the volumetric rate of this compensation because the experimental data on the magnitude of changes in the cerebral blood volume obtained by the method of intracranial electroplethysmography can be expressed only in relative units. However, it is obvious that these limitations may affect the compensation of processes whose duration is several seconds.

Let us now attempt to evaluate the volumetric possibilities for this mechanism of compensation of the cerebral blood volume.

It follows from the diagram shown in figure 25 that the magnitude of the volumetric limitation of compensation may be evaluated with the help of equation (11) if we trace the relationship between changes in the cerebral blood volume ΔV_{bl} and blood pressure ΔP_{bl} in the cerebrovascular system with increase in the cerebral blood volume due to the action of a negative gravitational stress.

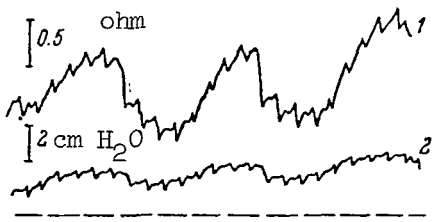

Figure 33. Pulse and respiratory waves of an intracranial EPG (1) and intracranial pressure (2) in a cat. Acute experiment.

Time marker - 1 sec.

When equilibrium is reached in the system, i.e., some time after a change in body position, the relationship between change in the cerebral blood volume and change in blood pressure will be determined by the following expression

$$\Delta V_{bl} \simeq \alpha \Delta P_{bl}. \qquad (12)$$

The equation that determines the relationship between ΔV_{bl} and ΔP_{bl} was derived by assuming that the volume compensation possibilities are unlimited. If this proposition is valid, there must be a direct proportionality between changes in ΔV_{bl} and ΔP_{bl} when α is constant. When the volumetric resources of the cranial or spinal cavity are depleted, the direct proportionality between ΔV_{bl} and ΔP_{bl} is impaired.

Now let us turn to the results of the experiments. In order to trace the proportionality between the blood pressure changes in the cerebral vessels and the cranial cavity blood volume, we used negative longitudinal gravitational stresses which could be produced very quickly. To decrease the effect of active /84 reactions by the cerebrovascular system under such stresses the experiments were conducted on deeply anesthetized animals.

The results obtained in this series of experiments are shown in figure 34. As we can see from the graph, for accelerations of up to 1.0-1.5 G there is a direct proportionality between the intensity of the stress and changes in the cranial cavity blood volume. In other words, the experimental and calculated data coincide; but as the stress is increased further, the direct proportionality between ΔV_{bl} and ΔP_{bl} is disrupted and V_{bl} no longer increases. This indicates that the reserves for this method of compensation are exhausted. What is the reason for this result?

It follows from the diagram shown in figure 25 that the excess volume of the CSF released from the cranial cavity when its blood volume increases shifts into the spinal cavity. Therefore, the volumetric possibilities for this mechanism of compensation depend, firstly, on the capacity of this cavity and, secondly, on the capacity of the reserve spaces in the cranial cavity.

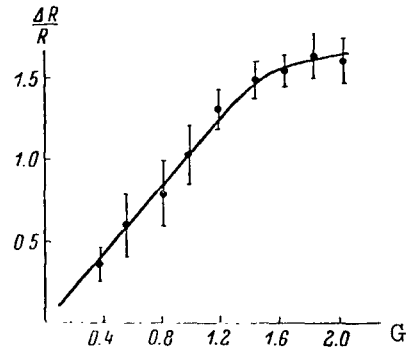

Figure 34. Relationship between relative changes in the level of the intracranial EPG ($\Delta R/R$) and intensity of longitudinal accelerations (G). Acute experiments on cats in a state of deep ansethesia. The vertical lines show the 95 percent reliability intervals of the average values.

In regard to the first factor, it is widely believed that under normal conditions the spinal cavity does not block the entry of CSF from the intracranial cavity. This opinion is based on the fact that the spinal cavity is somewhat elastic due to the cartilaginous connections between the vertebrae. In addition, the capacity of the CSF spaces has certain reserves by change in the volume of the extensive venous sinuses. This point of view is maintained by Hürthle (1927), Kedrov and Naumenko (1954), Fridman (1957), Moskalenko and Naumenko (1957, 1959a, 1964), and other authors.

It was confirmed by Gilland (1965), who recorded the relationship between the volume of physiological solution introduced into the spinal cavity and the elevation of spinal pressure in patients with a complete spinal block at the level of the cervical vertebrae. Gilland showed that the spinal cavity has marked distensibility.

The role of the second factor which limits the volume rate of the mechanism of compensation under study: the restricted capacity of the reserve CSF spaces /85
in the cranial cavity--may be evaluated by comparing the results of the investigations of Rosomoff and Zugibe (1963) with the data on the volume of CSF in the subpial spaces and cisterns presented by Shamburov (1954). Rosomoff and Zugibe established that the total volumes of the blood and CSF in the cranial cavity are equal, respectively, to 2.26 and 8.92 percent of the total volume of this cavity. According to Shamburov, 40 to 60 percent of the CSF is contained in the subpial spaces and cisterns, which corresponds to 3.6-5.0 percent of the total cranial cavity volume. From this we can conclude that the volume of blood in the cranial cavity may increase by not more than a factor of 2.5-3 if such increase is due to the movement of the CSF from the subpial spaces and cisterns. Under actual conditions it seems that part of the CSF still remains in the subpial spaces and cisterns. Therefore, the maximum possible increase in the cerebral blood volume can hardly exceed 100-150 percent. Thus, it is fair to conclude that the reserves for the compensation of changes in the cranial cavity blood volume due to release of the CSF into the spinal cavity are apparently limited by volume of the reserve CSF spaces in the craniocerebral cavity.

In concluding this examination of the possibilities for compensation of cerebral blood volume changes by release of the CSF into the spinal cavity, it can be stated that this mechanism of compensation permits substantial changes in the cerebral blood volume but the rate of change is quite limited.

Section 3. Relationship Between The Cerebral Blood Volume And Intracranial Pressure

Analysis of the diagram shown in figure 25 reveals that there are two mechanisms of compensation of changes in the cerebral blood volume. The first is associated with the release of a certain volume of venous blood from the cranial cavity, while the second involves the movement of CSF into the spinal cavity. These mechanisms have different functions: one is characterized by a high rate of compensation but small volume capabilities, while the other is characterized by a relatively low rate of compensation but a high capacity. The common feature of these two mechanisms is the participation of the CSF. Thus, CSF pressure and dynamics may give us significant information on the action of these two mechanisms and consequently on the state of the cerebral blood flow under various conditions.

Accordingly, in the present section, we shall consider the relationship /86
between the cerebral blood volume and intracranial pressure. This matter is of interest because intracranial pressure can be easily recorded in experiments on animals as well as on man under clinical conditions.

The data on the relative effect of arterial and venous pressures on intracranial pressure quite extensive. Duomarco and Rimini (1947) showed that pressure in the cerebral venous system, and intracranial pressure are the same and both vary with the position of the body. Ryder et al. (1953) noted that intracranial pressure is maintained by the pressure in the large veins of the cranial cavity. The authors observed a parallelism between changes in sigmoid sinus pressure and intracranial pressure. According to Lassen (1959), intracranial pressure has the same value as pressure in the veins of the pia mater.

Bowsher (1953) and Vasilevskiy and Naumenko (1959) think that the level of intracranial pressure basically depends more on venous than on arterial pressure. There are also points of view and quite convincing facts that CSF pressure depends on the level of the arterial pressure. The relationship between changes in arterial pressure and CSF pressure were noted long ago by Navalikhin (1874) and Falkenheim and Naunym (1887). This association was confirmed by later investigators (Scheinberg, 1958; Ryder and Espey, 1952; Ryder et al., 1952; Hodes et al., 1953; Shenkin and Novac, 1954; others). They also mention a relationship between the level of intracranial pressure, cerebroarterial tone, and intensity of the cerebral blood flow.

Attention should also be given to the data which show the absence of a relationship in some cases between cerebroarterial tone and the level of intracranial pressure. This was shown by Soklov and Pukhidskiy (1939), who emphasized, however, that dilatation of the arteries is always associated with an increase in CSF pressure while their constriction is associated with its decrease. Zlatoverov (1955), using a brain-heart-lung preparation, showed that sharp rises in arterial pressure induce a rise in intracranial pressure, but a drop in the systemic arterial pressure does not cause a drop in the CSF pressure.

A clear example of the absence of a parallelism in the changes in arterial and CSF fluid pressures, but one which indicates a close connection between changes in the CSF and venous pressure, comes from experiments on dogs in which /87
pressure changes in these systems were recorded during stimulation of the vagus nerve (Moskalenko and Naumenko, 1964). During cardiac arrest the systemic arterial pressure system dropped sharply while the intracranial and venous pressure decreased insignificantly. The pulse fluctuations vanished but the respiratory waves persisted (fig. 35). When cardiac activity was restored and arterial pressure rose for a short time period, the CSF and venous pressures increased simultaneously.

Thus, the data now available show that the level and changes in intracranial pressure depend first on the level and changes in pressure in the cerebral venous system, which determines the minimum value of the intracranial pressure.

A factor of secondary importance is arterial pressure, which affects the level of intracranial pressure both in the direction of its increase as well as in the direction of its decrease, but not below a level dictated by venous pressure.

In addition to the vascular factors which affect the intracranial pressure, we must also take into account the role of the processes of secretion and resorption of CSF. Change in the volume of the CSF produced by change in the relationship between the rate of its secretion and resorption, may sometimes have a profound effect on intracranial pressure. Thus, McQueen and Jeanes (1964) showed that when urea is introduced into dogs thereby producing dehydration of the brain, the intracranial pressure drops on the average from 120 to 64 mm H_2O.

However, under normal conditions the rates of secretion and resorption of the CSF are small and the correlation between them changes very little. This is responsible for a certain constant constituent of the intracranial pressure

level which serves as a background for changes in the CSF pressure which are determined by the arterial and venous pressures.

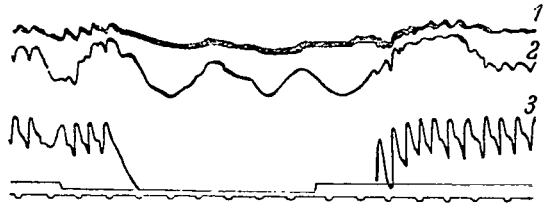

Figure 35. Changes in intracranial pressure (1), blood pressure in the sagittal sinus (2), and arterial pressure (3) when the vagus nerve is stimulated. Acute experiment on dogs.

Time marker - 1 sec.

All the material examined indicates that intracranial circulation is in a constant state of dynamic interaction with the CSF. As shown above (page 65), the relationship between changes in the blood volume and CSF volume in the closed cranial cavity, at any moment of time, is determined by the expression /88

$$\Delta V_{bl} + \Delta V_{csf} = 0. \qquad (13)$$

The relationship between blood pressure and CSF pressure is more complex:

$$\Delta P_{csf} = f\left(\Delta P_{bl}, \frac{\partial \Delta P_{bl}}{\partial t}\right). \qquad (13a)$$

Equation (13a) reflects the total effect of the arterial and venous systems on the CSF pressure. However, these systems have different structures and we should expect, therefore, that their relative effect on the CSF pressure will not be the same. To understand the reason for the different effect of pressure changes in the arterial and venous systems on the CSF pressure, we shall examine the characteristics of the interaction of each of these systems with the CSF system. It is evident from the diagram shown in figure 25 that the effect of blood pressure changes in the cerebrovascular system on the CSF pressure is achieved in the following manner: change in blood pressure → change in the cerebral blood volume → primary change in the CSF pressure → change in the CSF volume within the cranial cavity → secondary change in the CSF pressure, fluid.

According to this diagram the effect of blood pressure changes in the arterial and venous systems on the CSF pressure is mediated by volume changes in each of these systems.

Arterial blood pressure in the cerebrovascular system is high. In the arteries at the base of the cranium it is 70-80 percent of the average arterial pressure (Feruglio, 1954; Kotel'nikov, 1962). In the medium-sized and small pial arteries the pressure drops 40-50 percent (Symon et al., 1963). Therefore, intravascular pressure in the arteries ensures the maximum blood volume of the system for a given elasticity of the vascular wall; under these conditions the arteries have a circular cross section. In this case, when the tone of the arteries is constant, the relationship between changes in the volume of the arterial system and the blood pressure in it is approximately determined by the expression

$$\frac{\Delta V_a}{V_a} \cong \alpha_a \frac{\Delta P_a}{P_a}, \qquad (14)$$

where α_a is the dilatation coefficient of distension of the arterial wall. It will be remembered that the walls of the cerebral arteries are thinner than those of the same caliber arteries in other parts of the body, which affects the values /89 of α_a.

Since the value of α_a is small, the transmission of arterial blood pressure to the CSF fluid must result in a substantial reduction. The extent of this reduction apparently depends on the tone of the arteries (fig. 36).

Unlike the situation in the arterial system, the blood pressure in the cerebral venous system is low. According to Belekhova (1958), the average blood pressure in cerebral sinuses in cats and dogs is of the order of 10 cm H_2O. Similar values are cited by Lassen (1959). In view of this rather low internal pressure, the venous system is far from being filled with the maximum amount of blood, so that the cross section of large venous trunks has the form of an ellipse rather than of a circle. The venous sinuses are known to have cross sections which differ substantially from that of a circle. For this reason a change in the blood volume of the venous portion of the cerebrovascular system does not require much force because change in the value of the venous system is not caused by change in the perimeter of the vascular wall--only the shape of the vessels is changed (fig. 36). Consequently, the transmission of venous blood pressure to the CSF must take place with much smaller losses than the transmission of arterial blood pressure. As we saw above, this is confirmed by a great amount of experimental data. The correlation between blood pressure changes in the cerebrovascular system may be expressed by the following equation

$$\Delta P_{csf} \cong K_t \Delta P_{bl}, \qquad (14a)$$

where K_t is the pressure transmission coefficient. For the arterial system, K_t has a value of the order of 0.1 while for the venous system it is close to 1. According to equation (13a), K_t also depends on the rate of change in P_{bl}.

As is evident from equation (10), a factor which affects the CSF, in addition to arterial and venous pressures, is the elasticity of the spinal cavity and the conditions for the release of the CSF in it.

Thus, the CSF pressure and dynamics during various reactions are determined both by the balance between the blood-pressure level in the cerebral vessels and /90 their tone and by the state of CSF release into the spinal cavity and the elasticity of this cavity. This is in agreement with the ideas of several investigators (Ryder et al., 1952; Hodes et al., 1953; Shenkin and Novac, 1954) on the relationship between the CSF pressure spinal fluid, and the state of cerebral blood flow because the latter depends on the same factors as the CSF pressure. However, this relationship is not clear because for example, an increase in the cerebral blood volume in relation to the factors which produce it may either improve or impair the cerebral circulation.

The characteristics of the relationship between the dynamics of the CSF pressure and its release into the spinal cavity throw light on the role of the CSF in protecting the cerebrovascular system and brain tissue from various mechanical effects, as demonstrated by several investigations (Vasilevskiy and Naumenko, 1959; others). Indeed, when we have rapidly rising but short-lived disturbances which occur as a result of impact, shaking, coughing, sneezing, etc., the sharp reflex increases in intracranial pressure protect the cerebrovascular system from excessive dilatation and help to cushion these disturbances. This characteristic of the intracranial circulation also plays a protective role with respect to the brain when gravitational stresses act on the organism. In the vivid phrase of Lassen (1959), during such action the CSF acts as an "antigravity suit" for the brain. A similar idea has been expressed by other investigators. For example, Rushmer et al. (1947) believe that the CSF protects the thin walls of vessels in the pia mater from excessive dilatation when the intravascular pressure increases, while Wyburn (1960) calls the CSF a special "water suit" which protects the brain from mechanical irritations.

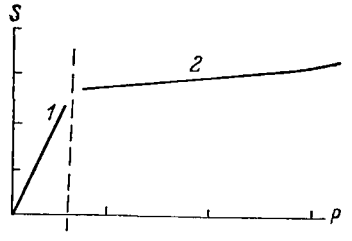

Figure 36. Relationship between intravascular pressure (P) and area of blood-carrying vessels (5). 1. Portion of relationship relating to absence of change in vessel perimeter; characteristic for changes in venous volume. 2. Portion corresponding to change in vessel perimeter; characteristic for change in arterial volume.

Analysis of mechanisms responsible for change in the CSF pressure in the cranial and spinal cavities and movement of the fluid between these cavities

has led us to conclude that the cerebral blood supply within certain limits does not depend on the level of the cerebral blood volume, or on the blood pressure in the cerebral vessels. This idea was recently confirmed by Kopylov (1965), who analyzed the structure of the cerebral venous system and came to the conclusion that there is "automatic" control of the cerebral blood flow without participation of the active mechanisms.

The nature of the association between the cerebral blood supply and arterial blood pressure may be explained in the following manner. Ignoring the active reactions of the cerebral vessels, the graph in figure 27, which shows the solution of equation (5), may be changed by substituting for the quantity W, which characterizes the total hydrodynamic resistance of the cerebral vessels, the intensity of the cerebral blood flow[1], its conjugate characteristic and by substituting for the volume of the arterial system the mean blood pressure in the cerebral arteries. The resulting relationship is shown in figure 37. The same figure shows the intracranial pressure curve. In this case the conditions for venous release are assumed to be unchanged. /91

As we can see in figure 37a, in the range of low blood pressure values in the cerebral vessels the CSF pressure is low and insufficient to ensure the release of the fluid into the spinal cavity. Therefore, in this region the CSF pressure and the intensity of the cerebral blood flow increase in proportion to the rise in blood pressure. Starting with certain blood pressure values (the left boundary of region b), the CSF pressure becomes high enough to ensure its compensatory release into the spinal cavity. Hence, the steepness of the change in CSF pressure decreases. In this region the intensity of the blood flow also ceases to increase because an increase in the volume of the arterial system is caused not only by the release of CSF into the spinal cavity but also by some increase in its pressure, which decreases the volume of the venous system and consequently increases it hydrodynamic resistance. The right boundary of region b corresponds to exhaustion of the possibilities for volume compensation of the cerebral blood volume due to the release of the CSF into the spinal cavity. A further increase in arterial pressure results in a substantial increase in intracranial pressure and decrease in intensity of the blood flow due to constriction of the cerebral veins.

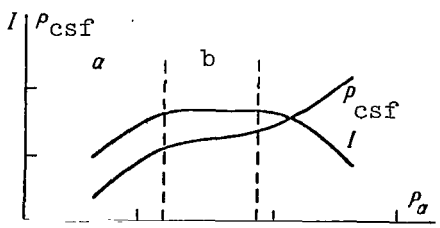

Figure 37. Relationship between the intensity of cerebral blood flow (I) intracranial pressure (P_1), and blood pressure in the cerebral arteries (P_a). Explanation in the text.

[1] Since we are taking into account here the possibility of CSF movement between the cranial and spinal cavities, the curve showing the relationship between the intensity of cerebral blood flow and of blood pressure (fig. 37) is the envelope of a family of parabolas corresponding to different volumes of CSF in the cranial cavity.

Thus, the curves presented in figure 37 show that because of the compensatory movement of the CSF the intensity of cerebral blood flow may not depend, within certain limits, on blood pressure changes in the cerebrovascular system or on the cerebral blood volume level. This conclusion is confirmed by experimental data obtained during a study of cranial cavity blood volume dynamics /92
under the influence of longitudinal accelerations (Moskalenko et al., 1964a, 1964b, 1964c).

As we pointed out above, there is a linear relationship between the cerebral blood volume and longitudinal acceleration in the case of man and animals under anesthesia of medium depth when the stress is increased to 0.4-0,6 G. This indicates an absence of active reactions by the cerebrovascular system during such stresses and, consequently, that with change in cerebral blood volume due to such stresses, the cerebral blood supply remains practically unchanged.

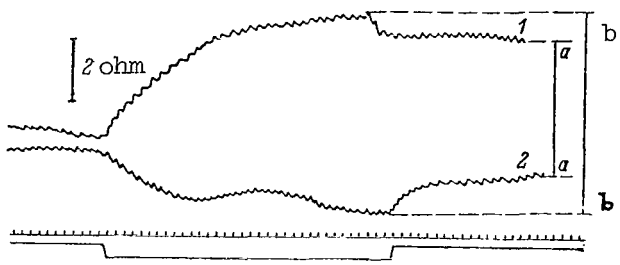

Figure 38. Dynamics of the cerebral blood volume level in man during negative (1) and positive (2) accelerations of 0.4 G after an extended stay in a horizontal position.

Time marker - 1 sec. Other symbols are explained in the text.

Furthermore, it has been observed in many experiments that the cerebral blood volume level under normal conditions is not entirely stable. Thus, when a longitudinal acceleration stress is applied to an animal that has remained a long time (at least 30 minutes) in a horizontal position, the cerebral blood volume level does not usually return to its initial value as happens after all repeated stresses in the same direction which follow each other after intervals of 1-2 minutes. It takes on a value intermediate between the initial value and the one observed at the moment when the reaction takes place (fig. 38). Comparison of the dynamics of the cerebral blood volume level after the action of positive and negative longitudinal gravitational stresses reveals that the cerebral blood volume may vary under normal conditions within certain limits aa (fig. 38) and yet not affect the cerebral blood supply.

There are also direct experimental proofs of the fact that the intensity of cerebral blood flow does not vary when the changes in arterial and venous pressures are not too sharp. Thus, Dewar et al. (1953) established that slight changes in arterial pressure which occur over a fairly long period of time are not /93
accompanied by changes in the cerebral blood flow. Similar effects were noted in human beings by Shroeder (1953) and Lassen (1959). Jacobson et al. (1963)

showed that the cerebral blood flow changes little during a slow pressure change in the superior vena cava. In this case changes in the CSF pressure had no effect on the results obtained.

These facts confirm the conclusion as to the existence of a mechanical stabilization of cerebral blood flow which was reached after analyzing the curves shown in figure 40. However, it should be borne in mind that the investigators cited did not record the cerebrovascular tone. Therefore, the effect they observed may well have been due to the active reactions of the cerebral vessels, because recent studies(Rapela and Green, 1964; Lassen, 1964; others) have shown that there exists a system of active automatic stabilization for the cerebral blood flow. This suggests that the relative stability of cerebral blood flow caused by the relationship shown in figure 37 is only one of the manifestations of the automatic regulation of cerebral blood flow. Such automatic self-regulation is also more-or-less ensured by the active reactions of the cerebral vessels.

The relationship between the values of the intracranial and arterial pressures permits us to define more precisely the concept of the rigidity of the cranial cavity. This concept is frequently used in works on intracranial circulation. By changing slightly the form of the diagram shown in figure 25, the interaction of the arterial system and the CSF may be represented in the form of a model consisting of two volumes: an internal volume with a wall dilatation coefficient α_1 and a volume surrounding it with a wall dilatation coefficient of α_2. The internal volume corresponds to the cerebroarterial system and is filled with blood under pressure P_1, while the external volume is limited by the brain case and is filled with CSF under pressure P_2. These forces will obviously be in equilibrium provided that $P_1/P_2=\alpha_2/\alpha_1$.

In view of the actual relationship between arterial blood and CSF pressures, it can be stated that $\alpha_2>\alpha_1$. In other words, the equivalent elasticity of the brain case under normal conditions exceeds the elasticity of the arterial wall. This equivalent elasticity of the cranial cavity is apparently made up of the dura mater and other elastic cranial formations[1]. It also depends on the conditions of blood release from the cranium and CSF release into the spinal cavity. /94

Thus, owing to the existence of above mechanisms of compensation of cerebral blood volume, the rigidity of the cranial cavity has rather symbolic significance, because under normal conditions the intact cranial cavity is equivalent to an elastic membrane.

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[1] The modulus of elasticity is a parameter which is reciprocal in value to the coefficient of dilatation. According to Flexner et al. (1932), the value of this coefficient for the dura mater is $4.0\text{-}4.5\times10^5$ dyne $\cdot cm^2$.

In summarizing this section we should like to emphasize once again that all the data considered here indicate that there is a constant dynamic interaction between the intracranial circulation and the CSF present in the cerebral and spinal cavities. This interaction makes it possible for there to be changes in the blood volume of the closed cranial acity, and thus permitting a physiological control of cerebral blood flow.

The characteristics of this interaction determines the relationship between changes in the total cerebral blood volume and the rate of change in blood pressure or vascular tone, as well as a degree of stabilization in the intensity of cranial blood flow during moderate fluctuations of blood pressure.

It will be noted that the indices considered--pressure in the arterial and venous systems of the brain, the elasticity of these systems and the elasticity of the cranial and spinal cavities--do not exhaust all the factors which affect the pressure of the CSF in the cranial cavity. For example, we did not discuss the effect of the rates of secretion and resorption of CSF on its pressure, assuming that under normal conditions the effect of this factor is insignificant when compared with the effect of other factors considered above. However, in certain isolated cases, particularly in pathological states, this factor may play a much more significant role.

Section 4. On Some Other Possible Mechanisms Of Compensation Of Changes In The Cerebral Blood Volume

The preceding sections have analyzed mechanisms of compensation of changes in the cerebral blood volume whose existence is determined by the diagram shown in figure 25. However, as we have already noted, this diagram reflects only the hydrodynamic properties of the intracranial circulation. Therefore, this section will present some facts which point to the existence of other mechanisms which cannot be predicted by analyzing the diagram shown in figure 25.

Other possible mechanisms are suggested by the data that we obtained when /95
investigating changes in the cerebral blood volume produced by the action of vasodilators, which affect both the cerebral and the spinal vascular systems to the same extent. In these cases compensation of the increase in the cerebral blood volume by the release of CSF into the spinal cavity is impeded.

It is common knowledge that one of the most effective vasodilators is carbon dioxide, which causes an intense dilation of cerebral vessels when its concentration in the blood is increased. Figure 39 shows changes in the blood volume level in the cranial cavity and spinal cord in a cat asphyxiated during an acute experiment (Moskalenko and Naumenko, 1959a). It is evident that soon after the start of the action, increase in cranial cavity blood volume resulted in the release of CSF into the spinal cavity. However, several minutes later the spinal cavity blood volume also began to increase.

We obtained these facts on the simultaneous increase in the blood volumes of the cranial and spinal cavities in collaboration with A. I. Naumenko using other vasodilators (nitroglycerin, diuretin, histamine). When these substances

act, the following pattern occurs, as in the case when CO_2 is inhaled: at first there is a reciprocal relationship between the changes in blood volumes of the spinal cavities, but then the spinal cavity blood volume also begins to increase.

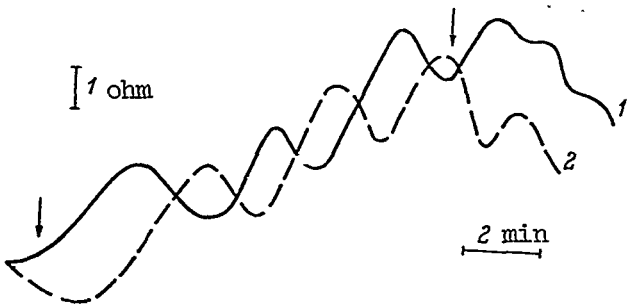

Figure 39. Change in the blood volume of the intracranial (1) and spinal (2) cavities of a cat during asphyxiation. Acute experiment. Arrows indicate the beginning and end of suffocation.

At the start of the reaction, the nature of blood volume changes in the cranial and spinal cavities is consistent with the mechanism of compensation of changes in the cerebral blood volume based on the diagram in figure 25. However, the second phase of the reaction, simultaneous increase in the blood volume of the intracranial and spinal cavities, shows that this compensation takes place in some other way when there is a simultaneous action on the vascular system of the brain and of the spinal cord. /96

During the dozens of years when intracranial circulation was investigated, several possible mechanisms of compensation were suggested. Some of them, for example the assumption that perimeningeal fat and cerebral substance become compressed during the increase in intracranial pressure, are obviously untrue. The assumption of compensatory resorption of CSF into the venous system when the cerebral blood volume increases (Bowsher, 1958) and release of the CSF into the subarachnoid sheaths of the craniocerebral nerves appears more realistic.

The possibility of the first of these methods of compensation is supported by data on the existence of relatively active resorption of the CSF into the venous system when the fluid pressure increases (Guttman, 1936; Alov, 1953; Bedford, 1955; Vasilevskiy and Naumenko, 1959; others). Bowsher (1958) found that increasing intracranial pressure by pressing the abdomen accelerates the entry of Na^{24} (introduced into the cisterna magna) into the blood.

The resorption of CSF when the cerebral blood volume is increased should result in fairly rapid release of the CSF when the blood volume decreases or when the vasodilatory reaction ceases. However, CSF is known to be produced rather slowly. The results of measuring the value of CSF secretion presented by differnt authors differ substantially; for example, for dogs the values obtained range from 8 to 300 ml/day (Dixon and Halliburton, 1916; Frazier and Peet, 1914;

Alov, 1950; Vasilevskiy and Naumenko, 1959). Even if we take the maximum value, we find that the production of CSF spinal fluid is not more than 0.2 ml/min because the volume of the CSF in the subpial spaces, cisterns, and cerebral ventricles of dogs is 12-18 ml (Fridman, 1957). Thus, during a period of 1 minute not more than 1 to 2 percent of the volume of CSF is produced. This calculation shows that such a mechanism of compensation is a rather slow. Nevertheless, we cannot exclude the possibility that this mechanism plays a role in compensating changes in the cranial cavity blood volume when CO_2 and other vasodilators act. The reaction to these vasodilators develops over a relatively long period of time. The restoration of the initial blood volume level also takes place slowly.

During the vasodilator reactions which affect simultaneously the vascular systems of the brain and the spinal cord, a role may be played by a compensation mechanism such as the release of the CSF into the subarachnoid sheaths of the craniocerebral nerves, which, according to Ahrens (1913), are a continuation of the subarachnoid space of the cranial cavity. Vasilevskiy and Naumenko (1959) showed that radioactive isotopes introduced into the subarachnoid space penetrate rapidly into the sheaths of the craniocerebral nerves. However, the capacity of this seems quite limited. /97

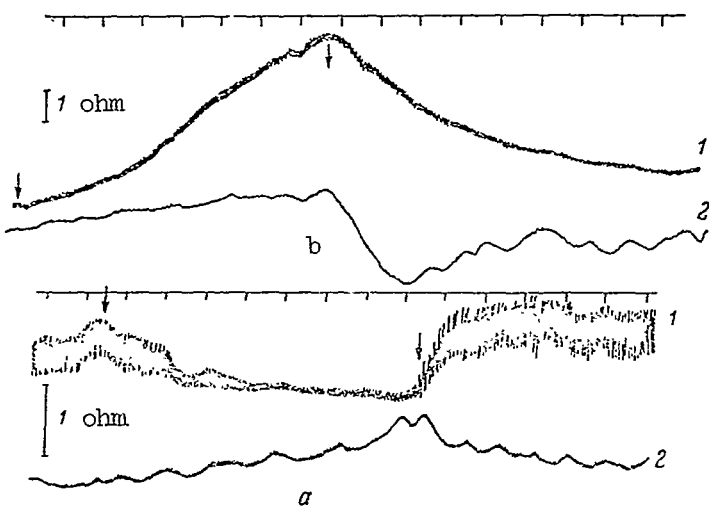

Figure 40. Change in the blood volume of deep cerebral vessels (a) and pial vessels (b) and in oxygen tension of the corresponding parts of the brain in man when a gaseous mixture containing 10 percent CO_2 is inhaled. 1. blood volume; 2. oxygen tension. The arrows indicate the beginning and end of the action.

Time marker - 10 sec.

During such reactions some increase in the cerebral blood volume may also take place due to distension of the dura mater in the places where it is not immediately adjacent to the cranial bones and also due to the dilatation of other elastic formations in the cranial cavity.

An interesting pattern which points to the possibility of still another method of compensating changes in the cerebral blood volume when there is a simultaneous dilatation of both the cranial and spinal vessels was noted when a comparison was made of the EPG curves recorded from surface and implanted electrodes in man during the inhalation of a gaseous mixture containing 10 percent CO_2. While the EPG recorded from subdural electrodes reflects a substantial increase in the blood volume of the pial vessels, the EPG recorded from deep electrodes shows some decrease in the blood volume of the vessels of the white and gray matter (fig. 40). In other words, compensation of the blood volume pial vessels in inhalation of CO_2 may be effected in part by a decrease in the blood volume of the deep cerebral regions. It is difficult to say whether the latter decrease is the result of mechanical compression due to an increase in the blood volume of the pial vessels or whether it is due to special active reactions of the internal cerebral vessels to this stimulation. In any case, however, we cannot rule out the possibility that this is still one other method of compensatory changes in the cerebral blood volume. /98

Section 5. Simulation Of The Intracranial Circulatory System

The material presented in the preceding sections shows that the behavior of the intracranial circulatory system is in agreement with the diagram shown in figure 25. However, we have thus far considered only particular relationships observed in experiments. To demonstrate the applicability of the proposed diagram, we shall have to determine to what extent it agrees with the system under study as a whole. One possible approach to such an evaluation is to investigate a model of the intracranial circulation in which the characteristics of the system shown in figure 25 could be programmed. This method of verifying and elucidating circulatory mechanisms is becoming increasingly popular. Analog models of individual elements of the circulatory system are very common (Noordergraaf et al., 1963; Zlatoverov, 1964; Clark et al., 1965; others) because by using simulation it is possible to verify certain hypotheses as well as to study the parameters of the systems which cannot be investigated in experiments on real objects. It also uncovers new problems for further investigation. Therefore, the simulation of the intracranial circulation should also be looked upon as preparation for the further investigation of this part of the vascular system.

In this connection let us now consider one possible method. In the simulation of the intracranial circulatory system that we carried out jointly with V. V. Menshutkin we used the diagram in figure 25 as the basis for the model, taking into account the following characteristics. /99

1. The intracranial cavity has a certain volume filled with CSF and this volume changes with change in the volume of the cerebrovascular system due to

certain limited elastic deformations of the dura mater and other elastic cranial formations and as well as to the release of the CSF into the subarachnoid sheaths of the craniocerebral nerves.

Part of the CSF may overflow from the cranial cavity into the spinal cavity and back.

2. The volumes of the arterial and venous blood in the cranial cavity depend on the relationship between the arterial, intracranial, and venous pressures and on the elasticity of the arterial and venous walls.

3. Aside from the hydraulic resistance of the capillaries, which in the present work is assumed to be constant, the intensity of blood flow through the brain depends on the difference in pressures between the flow into the capillaries and outflow from them. These pressures are determined both by the arterial and venous pressures at the entry to the cranial cavity and by the hydraulic resistance of blood vessels. This in turn is significantly related to the cross section of these vessels and consequently to the volumes filled with blood.

4. It is assumed that the volume of fluid in the spinal cavity may change due to the elasticity of this cavity and to fluctuations in the volume of the venous vessels situated in this space. The dynamics of these quantities is significantly related to the pressure of the CSF in the spinal cavity and to the blood pressure in the venous system of this cavity.

Since information on the system being simulated is basically of a qualitative rather than a quantitative nature, it cannot be easily described at present. The use of analog devices is also undesirable because they are bulky and not very flexible. We therefore selected the method of functional and logical simulation (Novic, 1965) which makes it possible to describe a functionally complex system without exhaustive information on the characteristics of all its elements. In this particular problem it is necessary to evaluate only the general nature of the dynamics of the system under various external conditions.

Let us consider the system as a finite automatic device (Glushkov, 1962). Let us further assume that certain structural elements can be isolated in the system, i.e., that the system can be presented as a composite one consisting of a finite number of automatic devices.

In this treatment it is assumed that all the variables contained in the system must be determined on the basis of finite sets. In other words, each variable may assume only one value from a set of predetermined discrete values. /100
These values are assigned only numbers (using the octonary system for the convenience of subsequent programming) in order of increasing quantity. The scale and physical units of measurement are unimportant in this approach.

The block diagram of the model is shown in figure 41. If we consider the system to be a single finite automatic device, then its state is determined by the states of the component automatic devices Ac, Vc, Lc, Qc, Vs, Ls, Ics in combination. The input quantities are the values of the arterial pressure pa,

venous pressure pv in the cranial cavity, and the venous pressure pq in the spinal cavitv at a given moment. The output quantity is the flow of blood through the brain Q. Consideration of the system in the form of a single finite automatic device would naturally be extremely cumbersome and impractical. For this reason the elementary automatic devices were kept separate.

The state of the automatic device Ac is determined by the relationship between the pressure in the arterial vessels and their volume. It is assumed here that the arterial vessels have a nonlinear deformation characteristic when the intravascular pressure is high (Savitskiy, 1956).

The automatic device Vc describes the behavior of venous vessels in relation to the venous and CSF pressures. The venous vessels are assigned the property of reacting passively to the difference between the external pressure ph and the internal pressure pv with a certain time delay.

The automatic device Lc simulates the relationship between CSF pressure in the cranial cavity, changes in the volume of the arterial and venous vessels, /101 fluctuations in intracranial volume, and CSF flowing over into the spinal cavity or in the reverse direction. The characteristics of the cranial cavity elastic deformations are assumed to be different with high and low CSF pressures.

The movement of CSF from the cranial cavity into the spinal cavity or back depends on the difference in pressures between the CSF in the cranial and spinal cavities ph-ps. Some amount of time is required to obtain a noticeable flow of fluid j when the pressure difference is constant. This indicates that the rate of flow of the CSF between the cranial and spinal cavities is limited. This time becomes smaller the greater the drop in pressure. After the external forces have ceasedto act, the flow of the CSF stops very quickly and the deceleration is less than the acceleration time. In the construction of a table for the transitions of the automatic device Ics, consideration was also given to the factthat the resistance to the flow in the direction of the cranial cavity is less than in the opposite direction. This is confirmed by data presented in table 5.

Changes in the volume of the spinal cavity in relation to pressure changes in it, fluctuations in the volume of the venous vessels, and overflow of the CSF from the cranial space are realized in the automatic device Ls. The spinal cavity is assigned the capacity for elastic deformations over the entire permissible range of distension, and the pliancy of this cavity is substantially higher than that of the cranial cavity.

It is assumed that the relationships which determine the changes in the state of the venous vessels in the spinal cavity (the automatic device Vs) are in principle analogous to the relationships which determine the changes in the state of the cerebral venous vessels (the automatic device Vc).

The operation of the automatic devices may be described by means of a matrix for the transitions or by means of a graph. As an example we present the graph of the automatic device Ac (fig. 42). Each state of the arterial vessels has corresponding values pa and wa. A total of 35 states is considered (43 in the

octonary system). The permissible transitions are designated by the arrows. For example, when the arterial pressure increases to 12, the automatic device passes from state 17 to state 7 while the volume of the arterial vessels increases to 7. On the other hand, when the arterial pressure remains constant, the automatic device goes into the stable state 20 from the same initial state.

The above simulation was carried out on the Minsk-2 electronic computer (Polenov Neurosurgical Institute in Leningrad). The block diagram of the program is shown in figure 43. The operator 1 introduces the program into the operational memory of the computer and then sends the parameters of the initial state to the operational units. Operator 2 transmits control in a definite sequence to operators controlling the transition of the individual automatic devices to the /10
next state. Thus, operator 3 prepares data on changes in the arterial pressure, as an input for the automatic device Ac. The input of the automatic device Vc is the difference between the venous and intracranial pressures (operator 4); the input of the automatic device Vs is analogous (operator 6), and this input takes into account the pressure in the spinal cavity. The input quantities for automatic devices Lc and Ls are the corresponding changes in the volumes of the cranial and spinal cavities and also the movement of the CSF between them (operators 5 and 7).

Operator 8 determines the state of the input for the automatic device Ics which depends on the difference in pressures ph-ps. The cerebral blood flow Q is the output of automatic device Qc whose input consists of data on the arterial and venous pressures and on the state of the cerebral venous and arterial vessels (operator 9).

After the state of the input of the next automatic device is prepared, control is turned over to the operator who seeks the corresponding element in the matrix for the transitions of the particular automatic device. Operator 10 reads the next line in the conversion table while operator 11 compares the initial state of the automatic device and state of the output with the data read from the table. If these coincide, the next state of the automatic device and the value of the output is remembered. If they do not coincide, operator 10 reads /103
the next line or lines until the required information is obtained. After this control is turned over to operator 2, which starts the automatic devices in the assigned sequence.

When all the automatic devices of the system go over to the next state, operator 2 transfers control to operator 12, which brings the system to a stop 14 if the input tables of the system (pa, pv, pq) are exhausted. Otherwise, control is turned over to operator 13. This operator sends the parameters of the new state of the system to the operating units, and the entire cycle is repeated.

The operation of the above model was investigated by solving several examples simulating actions that were very throughly studied in experiments. The law for change in the inputs of the model was assigned and the behavior of the individual elements was compared with the corresponding processes recorded in a real experiment. It was found that when the pressures at the inputs of the model corresponding to pulse fluctuations were changed, the model reproduced

the pulse fluctuations in CSF pressure in the cranial cavity and in the spine; these fluctuations were similar in shape to the curves obtained experimentally (fig. 52). The dynamics of the amplitude and shape of these fluctuations when simulating the action of positive and negative accelerations are consistent with the data obtained in real experiments if there are no active reactions of the cerebral vessels. The model also reproduces well the automatic regulation of the "intensity of cerebral blood flow" when the parameters of the "arterial" and "venous" inputs of the model are changed within certain limits.

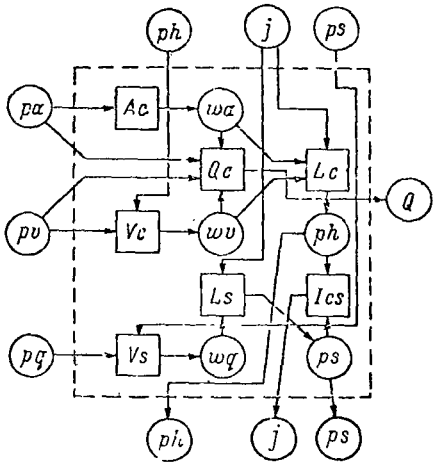

Figure 41. Block diagram of a model of the intracranial circulation represented as a composition of finite automatic devices.

Ac--automatic device responsible for change in the volume of the arterial system in relation to the blood pressure there; Vc--automatic device responsible for changes in the venous system volume in relation to the venous blood pressure and the CSF pressure in the cranial cavity; Lc--automatic device responsible for changes in the CSF fluid pressure in the cranial cavity in relation to the arterial and venous system volumes; Ls--automatic device responsible for changes in CSF pressure in the spinal cavity as in relation to CSF movement from the cranial cavity and in relation to the venous system volume in the spinal cavity; Qc--automatic device responsible for changes in the intensity of cerebral blood flow as in relation to blood pressure difference at the entry of the arterioles and exit of the venules; Ics--automatic device responsible for changes in the movement of the CSF between cranial and spinal cavities in relation to the differences in pressures in these cavities; pa, pv, pq--inputs of the automatic device--arterial and venous pressures in the cranium and spine; Q--output of the automatic device--intensity of cerebral blood flow; ph, ps--CSF pressure in the cranial and spinal cavities; j--CSF volume overflowing from the cranial cavity into the spinal cavity and back; wa, wv and wq--arterial and venous system volumes in the cranial cavity and venous system volume in the spinal cavity.

The model goes quickly into a stable closed cycle from any permissible initial state. This cycle corresponds to a definite level of fluctuations in the input quantities.

Thus, a comparison of data obtained with the model with the results of experiments on real subjects shows that the model can be tentatively used to explain the activity of the intracranial circulatory system and that, consequently, the ideas on which the diagram shown in figure 25 is based correspond to the true picture of the phenomena that occur in the system under study. /104

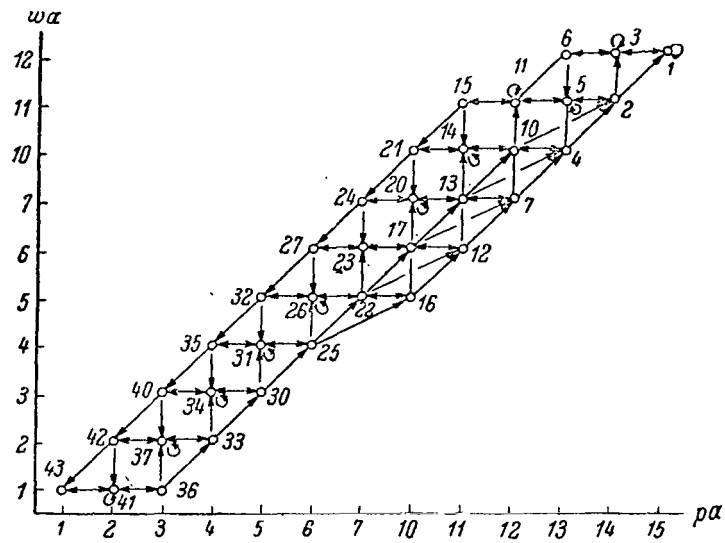

Figure 42. Graph of an automatic device Ac (in an octonary system). ta and wa are the pressure and volume of the arterial system, respectively. Other explanations are in the text.

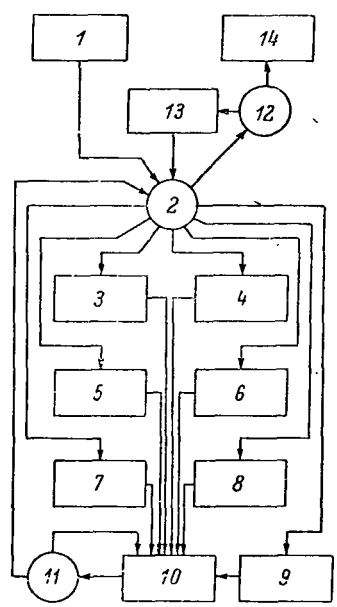

Figure 43. Block diagram of a program for simulating the system shown in figure 41 on a Minsk-2 computer. The explanation is in the text.

CONCLUSION

In setting out to elucidate the mechanisms of compensation of changes in the blood volume of the closed cranial cavity, we presented a simplified diagram showing the structure of the intracranial circulatory system (fig. 25) and on the basis of this diagram we suggested two probable mechanisms of such compensation.

Analysis of the available experimental data enabled us to prove the existence of two mechanisms and to determine their rate and volume capabilities. The agreement of the experimental data with the results of calculations and with simulation is grounds for assuming that the diagram shown in figure 25 correctly reflects the true picture of the hydrodynamic relationships between the fluids contained in the closed cranial cavity.

It follows from our data that the conditions of intracranial circulation do not differ from those of the circulation in other parts of the body and organs thanks to the mechanisms of compensation of changes in the cerebral blood volume. Indeed, according to the general ideas on the biophysics of the circulatory system (Beier, 1960), the blood volume level in any part of the body is determined by the relationship between the forces created by blood pressure which distend the vascular wall and the forces of counterpressure on the vessels produced by the tissues which surround them. The forces of internal pressure and counterpressure are directly proportional to each other. The intracranial circulatory system is also subjected to definite counterpressure by the CSF. The level of the cerebrovascular blood volume is determined by the relationship between the forces which dilate the intracranial vessels (blood pressure) and the forces of counterpressure (CSF).

However, the intracranial circulation has certain distinctive features. In the first place, the nature of the relationship between the internal dilating forces and counterpressure is such that it also depends on the rate of change in intravascular pressure. This relationship becomes apparent when blood pressure changes are rapid. In the second place, due to the movement of the CSF during slow changes in intravascular pressure, the change in cerebral CSF pressure is relatively small. Thus, the structural characteristics of the intracranial circulation as schematically shown in figure 25 are essentially equivalent to /105
some characteristics of the relationship existing between the forces of intravascular pressure and the forces of counterpressure on the intracranial vessels.

The data considered in the present chapter make it possible to describe the nature of some changes specific to the cerebral circulation which arise under the influence of accelerations. In describing these changes we shall rely only on an analysis of the diagram shown in figure 25, assuming that the activity of other parts of the cardiovascular system remains constant during this time.

As we pointed out above, when longitudinal accelerations act on an organism, the forces affecting the blood flow move in the same direction as the blood under the influence of perfusion pressure. Furthermore, additional forces parallel to the spine also act on the CSF there, causing it to move upward or downward. Therefore, when longitudinal accelerations are acting, we must expect, first, changes in the cerebral blood volume and secondly changes in the efficiency of the mechanisms of compensation of its blood volume.

In the case of negative accelerations which cause the cerebral blood volume to increase, the first mechanism is blocked. This affects first the compensation of rapid changes in the cerebral blood volume. At the same time the compensating release of CSF into the spinal cavity is somewhat impeded. As a result, when negative accelerations acting, along with an increase in the cerebral blood volume due to deterioration in the release of the blood from the cranium, we must also expect disturbances of the compensation of changes in the blood volume, particularly those forms of it caused by rapid processes to such as pulse waves. All of this gives us a basis for assuming that when negative accelerations are acting, there will be marked disturbances of the cerebral blood supply with all of the resulting consequences.

The action of positive stresses in accordance with the diagram shown in figure 25 will cause the cranial cavity blood volume to decrease while the efficiency of the mechanisms of compensation of changes in the blood volume increases. Therefore, disruption of the cerebral blood supply due to the impariment of blood flow will not be as pronounced as in the case of negative stresses. Compensation of changes in the cerebral blood volume during the action of positive accelerations will be more effective than under normal conditions.

Thus, specific changes in the intracranial circulation during negative accelerations will aggravate the disruptions in the cardiovascular system, whereas during positive gravitational stresses they will promote the compensation of the observed changes. /106

As for transverse accelerations, analysis of the diagram shown in figure 25 makes it difficult for us to expect substantial changes in the intracranial circulation. Presumably such action will somewhat affect the efficiency of the mechanisms of compensation of the cerebral blood volume because transverse accelerations result in a redistribution of the fluids in the cranial cavity.

Consequently, during transverse accelerations changes in the intracranial circulation depend primarily on the effect of this factor on the central portions of the cardiovascular system, whose peculiarities will be considered below.

It is possible that in the processes that take place the intracranial circulation during gravitational stresses a part is played by other mechanisms of compensation of changes in the cranial cavity blood volume. These mechanisms were briefly discussed in section 4. However, in the subsequent chapters we shall show that the principal role in the compensation of changes in the blood volume of the closed cranial cavity in man and animals under normal conditions and during gravitational stresses is played by the very mechanisms suggested by the diagram.

CHAPTER 3. FEATURES OF INTRACRANIAL PULSATION UNDER NORMAL CONDITIONS AND DURING INCREASED GRAVITY

It is known that one of the basic mechanisms of the circulatory system is /107
the pulsating nature of blood flow, which is conditioned by the rhythmical beat of the heart. Pulsating fluctuations of arterial pressure cause changes in the pooling of blood in parts of the body and organs as well as variations in the rate of blood flow in vessels. According to the data of Wiggers (1954) and Savitskiy (1956), pulsation is propagated via the vascular network down to the capillary network; in some cases, even capillary blood flow has a pulsating character. Pulsating fluctuations of blood pooling in parts of the body and organs not in direct proximity to the heart which can be recorded plethysmographically (including electroplethysmography or EPG) correspond in form to fluctuations in arterial pressure as a rule (see fig. 44).

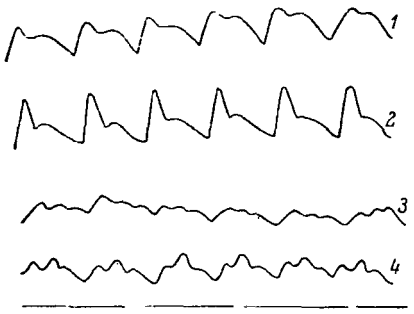

Figure 44. Features of the pulse waves of an intracranial EPG and the intracranial pressure in a dog compared to EPG pulsations and arterial pressure in a rear extremity.

Acute test. 1. EPG of a rear extremity; 2. arterial pressure in the femoral artery; 3. an intracranial EPG; 4. intracranial pressure. Duration: 1 sec.

It is to be expected that the pulsating nature of blood flow is also characteristic of the intracranial system of blood circulation. However, the question of pulsation in the hermetic cavity of the cranium is one of the most controversial problems in the physiology of intracranial circulation.

For many decades, the existence of cerebral pulsation was considered to be established, based on observations of animals with exposed brains (Quincke, 1872; Richt, 1846; Pirogov, 1964; Nagel', 1889; Verigo, 1905; Hürthle, 1927; Sepp, 1928). During cerebral pulsation, periodic fluctuations in intracranial pressure were recognized which could be accompanied by changes of cerebral blood pooling.

The assumed presence of cerebral pulsation was contradicted by a multitude of in vivo visula observations of small vessels, arterioles, and capillaries of the brain (Donders, 1851; Ackerman, 1858; Navalikhin, 1874; Leyden, 1886; Riser, 1936; Forbes and Cobb, 1938; Alov, 1950 and others). These observations showed that when the cranial cavity was closed blood flow in arterioles and capillaries /108
was uniform and did not undergo any surging or acceleration.

Recently, a number of authors (Klosovskiy, 1951; Sigward, 1954; Brain, 1957; Volobuyev, 1965 and others) have conducted experiments designed to observe cerebral pulsation when the brain cavity is closed. Here, Klosovskiy, using an "air bubble" method, Volobuyev, observing a patient with a cranial defect covered by

plexiglass, and Sigward, using contrast roentgenoscopy (X-ray spectroscopy) found that pulsation is absent in a closed cranial cavity. Brain arrived at the same conclusion.

Along with these investigations, a number of works have been published in which the answer to the question of cerebral pulsation has been positive (Kedrov and Naumenko, 1954; Bering, 1955; Naumenko, 1956; Beer et al. 1956; Belekhova, 1959; Moskalenko, 1961; Naumenko et al. 1962 and others). These authors observed pulsed fluctuations of blood pooling and CSF pressure in a closed cranial cavity, which indicated pulsed variations in the blood flow in cerebral vessels. However, the curves of the above fluctuations substantially differed in form from curves of the peripheral pulse (see fig. 44). This does not permit equating intracranial pulsation with the volumetric peripheral pulse, which to a certain degree discourages acceptance of the existence of pulsation in the closed cranial cavity.

Thus, there presently exist two points of view relative to the question of pulsation in the closed cranial cavity. One of these, which is based on data obtained by indirect methods of observing cerebral vessels, is negative. The other, which is based on data obtained by recording intracranial pressure and the intracranial EPG, is positive. In the most fundamental investigations involving intracranial pressure, Klosovskiy (1951) and Sigward (1954) on one hand and Kedrov /109
and Naumenko (1954) on the other do not analyze the reasons for the contradiction of data on the presence of cerebral pulsation obtained by different methods.

Because of this, in this chapter we will present an analysis of periodic variations in the intracranial circulatory system caused by pulse fluctuations in systemic arterial pressure and will attempt to clarify the question of the existence and features of intracranial pulsation under normal conditions and during the action of gravitational forces.

Section 1. The Pulsation of Cerebral Arteries

There exist data to the effect that blood flow undergoes substantial changes at the entry points of arterial trunks leading to the cranial cavity. Klosovskiy (1951) persuasively demonstrated that pulsed fluctuations of pressure in cerebral arteries are significantly decreased compared to pressure fluctuations in extracranial arterial trunks of the same size.

Using the method of Hürthle we obtained similar data during the simultaneous recording of pulsed fluctuations of blood pressure in the common carotid artery and in arteries of the cranium. As is evident in figure 45, the amplitude of pulsed fluctuations of blood pressure in cranial arteries is substantially decreased. In dogs and cats (according to our data), it is equal to 30-60 mm Hg, i.e., is decreased in comparison to the value of pulsed fluctuations of pressure in the carotid artery by a factor of 1.5-4.0. The form of these pulsed fluctuations also undergoes substantial changes, which are expressed in the spectrum of pulse curves.

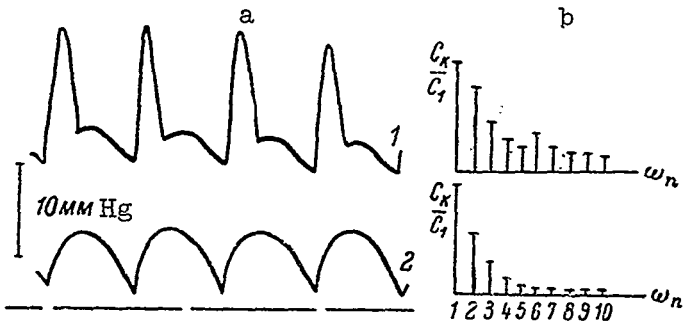

Figure 45. Changes in the parameters of pulsed fluctuations of blood pressure in arterial trunks leading to the cranial cavity.

Acute experiment on a dog according to Hürthle. a. pulse pressure waves in the carotid artery (1) and in arteries leading to the cranium (2); b. harmonic composition of these waves. w_n - ordinal number of harmonics; $\frac{S_k}{S_1}$ -relationship of the amplitude of "k-th" harmonic to the amplitude of the first. Duration: 1 sec.

What is the reason for the attenuation of pulse amplitude and a change in its spectral characteristics at the entry point of the artery into the cranium? /110 Klosovskiy (1951) considers that a decrease in pulsation is caused by the smoothing action of siphons (or bends) in the internal carotid and vertebral arteries where they enter the cranial cavity and also by the branching of the network of vessels of the pia mater. A like point of view is held by Savitskiy (1956). Recently, Sreseli and Bol'shakov (1962) demonstrated that a pulsating siphon is suspended by eight elastic strands in the sinus cavernosa, which can also result in additional attenuation of pulse fluctuations of arterial blood pressure in siphons. Such an influence by siphons in cerebral regional arteries is entirely possible, since the smoothing phenomenon of a pulsating flow of fluid in bent tubing is one of the classical laws of hydrodynamics.

However, there are a substantial number of objections against this point of view. For instance, it is known that the structure of the siphons of internal carotid and vertebral arteries vary significantly not only in various animals and man, but also in particular species. In a number of cases, these siphons are generally absent (Mikhaylov, 1965). Recently, Mchedlishvili and Ormotsadze (1962) established that regional arterial trunks by-pass the sinus cavernosa in rabbits. Therefore, the question arises that given anatomic formations play a substantial role in variations in the pulsed fluctuations of blood pressure where arterial trunks enter the cranium. This would suggest that variations in the magnitude of the attenuation of pulsed fluctuations of arterial pressure are also significant, particularly when compared to attenuation in such animals as the cat and rabbit. However, the latter is not confirmed by our data.

There are other possible reasons for changes in pulse fluctuations of pressure in the cerebral arterial system. One is that blood reaching the cranium feeds into a system of cerebral vessels whose total area surpasses the sum of the cross sections of the internal carotid and vertebral arteries.

An increase in arterial cross section in the cranial region must inevitably result in the smoothing of rapid changes in pressure and a decrease in their amplitude. A direct confirmation of this is the data mentioned above concerning the substantial gradient of mean pressure where arterial trunks enter the cranium.

Another possible reason for weakened pulsation in cranial arteries, and especially changes in its spectrum, is the unsynchronized arrival of pulse waves in vessels leading to the cranium from the internal carotid and vertebral arteries. Actually, the propagation rate of a pulse wave in arteries is 6-11 m/sec /111
(Lebedev, 1964; Medvedev, 1964) which means that in arteries leading to the cranium, the pulse wave does not arrive simultaneously since the length of vertebral arteries somewhat exceeds the length of the carotids. We have not composed accurate data on the relative disparity in the length of internal carotid and vertebral arteries. However, if the length of the latter is even 15-20 percent greater, the time difference in the arrival of a pulse wave from the system of internal and carotid arteries will be commensurate with the anacrotic duration of the arterial wave, which also can influence the form and amplitude of waves in arteries leading to the cranium.

Finally, one additional reason for the attenuation of pulse waves in cranial-based arteries is the damping action of the brain, i.e., the energy of pulse fluctuations of blood pressure in arteries leading to the cranium is dispersed by a slight displacement of the brain mass. The consequence of this is a decrease in pulse fluctuations and a smoothing of their form. Data supporting such a weakening mechanism of pulsation in cranial-based arteries show that under normal conditions even minor acceleration magnitudes, for instance longitudinal accelerations of 0.4-0.6 G, can occasionally produce a displacement of brain mass (Moskalenko et al. 1964). The occurrence of a pulsed displacement of brain mass permits the analysis of electropolarogram curves recorded from a point electrode implanted in cerebral tissue. Since blood flow in cerebral capillaries has been confirmed by in-situ microscopy, the presence of pulse waves on an electropolarographic curve can only be explained as the result of synchronous (relative to cardiac activity) displacements of brain mass relative to the electrode. The article by Naumenko et al. (1962) also indicates the occurrence of pulsed displacements of brain mass.

The above possible reasons for decreased amplitude and a transformation in the form of pulse fluctuations of blood pressure in cerebral arteries would thus indicate the substantial role played in this process by the anastomosis of the internal carotid and vertebral arteries--the circle of Willis, which suggests that this anatomic formation plays a significant functional role. The latter is interesting in connection with circle of Willis functions which were long ago discussed in the literature. In recent investigations devoted to this problem, methods of mechanical and electrical analog modeling have been employed (Avmak and Bering, 1961; Murray, 1964; Clark et al. 1965; Himwich et al. 1965). Thus far, however, there is no unanimous opinion as to whether the circle of Willis /112
is a simple anastomosis which increases the reliability of cerebral blood supply or whether this information plays a yet more significant functional role.

To determine whether the circle of Willis participates in the conversion of pulse fluctuations of arterial pressure, we conducted experiments using a hdyromechanical model of this formation.

The model was made of rubber tubing with an elasticity coefficient close to that of a vascular wall and connected to a system similar in structure to cranial arteries. A 15 percent difference in the length of the incoming tubes and double flexures modeling the siphons of the internal carotid arteries was introduced into the model. The pressure in this system was maintained at 100-150 mm Hg and fluctuated near this level by 15-20 mm Hg with a frequency of approximately 1 Hz, since the leading edge of these fluctuations was sufficiently abrupt. Electromanometers were included in the model in the same manner as during measurements of pulsations in arteries leading to the cranium in experiments on animals, i.e., one of the tubes was interrupted and the electromanometer was connected to its "central" and "peripheral" sections.

For purposes of comparing parallel experiments, investigations were conducted on a model consisting of a single rubber tube the length of which was equal to the sum of the length of all the components of the first model.

It was established that the amplitude and form of "pulse" fluctuations of pressure in the single rubber tube varied little despite its sufficiently great length (see fig. 46). However, in a system analogous to the structure of the circle of Willis and having the same total length, these fluctuations underwent substantial variations (see fig. 46) which were similar to those noted in experiments on animals. The elimination of the two bends or "siphons" from the model did not result in substantial changes in the parameters of recordable pressure fluctuations.

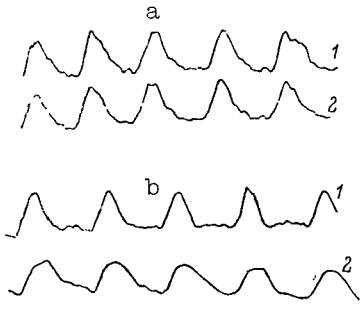

Figure 46. "Pulse Fluctuations" recordable on a model of the cranial-based vascular system. a. fluctuations at the beginning (1) and end (2) of a single tube; b. fluctuations at the input (1) and outlet (2) of a system of tubes simulating the circle of Willis.

These data permit the conclusion that pulse fluctuations of pressure in arteries leading to the brain are decreased in amplitude and altered in form because of the peculiarity of the structure of the circle of Willis. It is possible that the damping influence of the brain mass also plays a role in the process of fluctuation attenuation. /112

Section 2. Pulse Fluctuations of Intracranial Pressure

Pulsed fluctuations of pressure in the arteries of the intracranial cavity /113
cause analagous fluctuations in cerebrospinal fluid (CSF) pressure. Data on the magnitude of pulsed fluctuations of CSF pressure fluctations have been treated in many works (Becher, 1922; Ewig and Lullies, 1924; and others) but the most reliable data were obtained recently using electromanometers with small fluctuations in operating volume (Bering, 1955; Naumenko, 1956; Sicutery et al. 1959; Moskalenko, 1961; Naumenko and Vasilevskiy, 1962; and others). These data showed that the amplitude of CSF pulse fluctuations in various animals under anesthesia falls within 2-10 mm H_2O; for man, the value is 20-40 mm H_2O.

Thus, pulse fluctuations of intracranial pressure are relatively minor. In comparing them to pulse fluctuations of pressure cranial vessels, it is observed that the transmission of arterial pressure pulse waves to the CSF takes place with an attenuation factor on the order of 6-10. The reason for such a significant attenuation of pulsation amplitude is not difficult to comprehend considering the features of the interaction of fluid media in the closed cranial cavity, and in particular the difference in the elastic qualities of the cranial cavity and vascular walls demonstrated in a previous chapter (page 79).

In our opinion, Klosovskiy (1951) arrived at a negative conclusion relative to pressure pulsation in the heremetic cavity of the cranium namely because of the small magnitude of pulse fluctuations of fluid pressure. Klosovskiy attempted to detect pulsation using his own variation of the "transparent cranium" method. The experiment (on a dog) was designed such that an air bubble was introduced between the cranium and a plexiglass port replacing the cranial bone. In all cases, Klosovskiy assumed that a displacement in the air bubble and a variation in its radius indicated the development of pulsation when the hermetic seal of the cranium was broken. When the port was closed i.e., when complete hermetization was restored, a displacement and change in bubble radius instantly ceased.

In our opinion, Klosovskiy's method was distinguished by low sensitivity; furthermore, a fluctuation in fluid pressure would impart such insignificant dimensional variations to an air bubble that they would be impossible to observe even with a magnifying glass, not to mention the naked eye; therefore, they were unnoticeable in the photographs included in Klosovskiy's monograph (p. 344).

The small magnitude of fluctuations in the volume of an air bubble in /114
Klosovskiy's tests was confirmed by calculations. Starting with the law establishing the relationship between the pressure and volume of an ideal gas, we write:

$$-\frac{\Delta V}{V}=\frac{\Delta P}{P+\Delta P}, \qquad (15)$$

where V is the volume of the bubble; P is the initial pressure in the gas bubble equal to the sum of the initial fluid and atmospheric pressures; ΔP is the maximum value of pulse fluctuations of fluid pressure; and ΔV is the fluctuation in the volume of the air bubble.

Having established numerical values in formula (15), it develops that fluctuations in CSF pressure will cause relative variations in the volume of an air bubble not greater than 0.05 percent. Since Klosovskiy observed the displacement of the edge of the bubble, i.e., a change in its radius, the value of a change in the radius of a bubble, ΔR, as a function of a fluctuation in fluid pressure is calculated. Assuming the bubble is hemispheric, from formula (15) it is not hard to arrive at:

$$\frac{\Delta P}{P+\Delta P}=\frac{3\Delta R}{R}+\frac{3\Delta R^2}{R^2}+\frac{\Delta R^3}{R^3}. \tag{16}$$

Disregarding the higher stages of this equation, i.e., assuming an increase in a change in bubble radius, we arrive at:

$$\frac{\Delta P}{P+\Delta P}\cong\frac{3\Delta R}{R}. \tag{17}$$

Even in approximate calculations yielding obviously exaggerated values, it develops that $\frac{\Delta R}{R}$ does not exceed 0.01 percent. This means that when a bubble diameter is 0.5 mm, a decrease in diameter would not exceed 0.0003 mm or 300 Å. It is quite obvious that such a decrease in bubble dimension is impossible to observe visually even then increases are significant.

The microscopic variations in the volume of an air bubble can be recorded by varying Klosovskiy's method somewhat. In our modification of his method, the bubble 1 (figure 47) is placed not beneath the opening but in a transparent tube 2 hermetically attached to the subarachnoid space of the brain. The fluid 3, limiting the air bubble on one side, was stained with a dark color. It was impossible to observe visually the movement of the meniscus of the fluid; however, if a light soure 4 is placed on one side of the tube and a photoelement 5 on the other, these microscopic movements of the meniscus alter the exposure of the photoelement, causing electrical signals therein which can be recorded by a cathode oscillograph (fig. 48) after a 10^3 amplification.

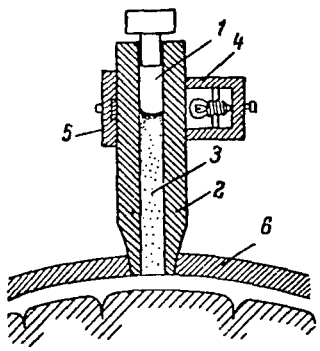

Figure 47. Construction of a photoelectric cell for recording pulse variations in the volume of an air bubble when the cranium is hermetically sealed. 1. air bubble; 2. tube; 3. stained fluid; 4. light source; 5. photoresistor; 6. cranial bone.

Figure 48. Pulse fluctuations of the volume of an air bubble 1 simultaneously recorded with a piezogram of arterial pulse 2. Acute test on a cat. Duration: 0.1 sec.

Thus, a slight modification of the "air bubble" method makes it possible to confirm the existence of periodic fluctuations of fluid pressure. /115

The development of significant movements of an air bubble when opening the aperture of a "transparent cranium," used by Klosovskiy to enhance intracranial pressure pulsation by disrupting the hermetic seal of the cranial cavity, has another origin. Calculations using formal (17) indicate that for such changes (nearly 70 percent) in the volume of an air bubble to be possible, fluctuations in CSF pressure on the order of 1000 cm H_2O (nearly 800 mm Hg) would be required, which is obviously impossible. Therefore, the reason for the change in bubble radius when the hermetic seal of the cranium is interrupted can be found in changes of form under the action of asymmetric forces causing an increasing pressure differential close to the bubble. Actually, in a closed cranium the pressure on a bubble is uniform on all sides (fig. 49). The volume of the bubble in this case varies synchronously with pulse fluctuations of fluid pressure by extremely small but entirely recordable values as we indicated above.

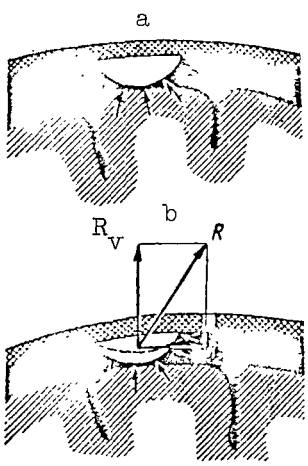

Figure 49. Diagram of forces acting on an air bubble when the cranium is closed (a) and open (b). Explanation in text.

On disruption of the hermetic seal of the cranium in the region of the bubble, a decrease in pressure at the opening disrupts the balance of forces, which results in the manifestation of a differentially acting force changing the form of the bubble and displacing it (fig. 49). This force is directed toward the opening: its horizontal component R_r displaces the bubble while the vertical component R_v compresses the bubble, thereby changing its shape. In this case, extremely minute fluctuations of fluid pressure (on the order of

1 cm H_2O) can cause noticable displacements and variations in bubble form while its volume remains practically unchanged.

The data obtained by Klosovskiy render questionable the types of changes /116
in intracranial pressure when the cranial seal is broken and whether qualitative changes in intracranial dynamics occur.

From the diagram in figure 25, it can be seen that an artificial opening in the cranial bones yields the additional possibility of compensatory changes in blood volume in the cranial cavity, the magnitude of which depends on the size of the opening. In the presence of such an opening, the compensation of pulse variations in blood volume within the cranial cavity is relieved and shifts in intracranial pressure must decrease. This agrees with our data (Moskalenko, 1961). In all cases, when the cranial aperture was opened in close proximity to the point of measurement, pulse variations in CSF pressure decreased somewhat (figure 50).

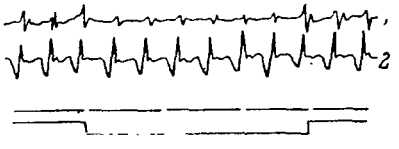

Figure 50. Effect of breaking and restoring the hermetic seal of the cranium on the amplitude of pulse fluctuations in intracranial pressure.

Acute experiment on a cat. 1. piezogram of intracranial pressure; 2. piezogram of the femoral artery (for comparison). Duration: 1 sec.

A decrease in CSF pulse fluctuations depended on the dimensions of the opening and its proximity to the point where intracranial pressure was measured.

Thus, hermetic disruption of the cranial cavity does not lead to a qualitative change in the hemodynamic relationships in the cranial cavity as Biedl and Reiner (1900) observed in noting that a trephined opening is but another addition to the many natural openings of the cranium.

We now consider another important parameter of pulse CSF shifts--their form. In the literature available to us, a consideration of the form of pulse fluctuations of pressure is lacking and there are only a few references to the effect that the form of these fluctuations is rather complicated (Becher, 1922; Ewig and Lullies, 1924; Belekhova, 1958; and others).

Our data confirm this position. The results of simultaneously measuring /117
pulse variations of intracranial pressure together with their evoked blood pressure fluctuations in cranial vessels and the spectral composition of these fluctuations are shown in figure 51. As is evident from the figure, the form of pulse fluctuations of intracranial pressure is somewhat more complicated when compared with pressure waves in cranial arteries; this finds its expression in the relative increase in the amplitude of higher harmonics in the pulse wave spectrum. In form, pulse curves of intracranial pressure (and also the intracranial EPG, as we will show later) are reminiscent of some types of sphygmogram and mechanical plethysmogram curves of rear extremities. However, this similarity is purely superficial in that pulse fluctuations recorded in the latter cases have

features of cardiac activity, while pulse fluctuations in the cranial cavity are caused by the pulsations of cranial arteries, as we saw in figure 45, and are relatively simple in form. Therefore, to explain the reasons for the complication in the form of intracranial pressure pulsation, we return to features of the hydrodynamic relationships in the cranial cavity shown in figure 25. According to that diagram, pulse fluctuations of intracranial pressure, including the amplitude of these fluctuations, depend not only on the characteristics of the imparting forces, i.e., fluctuations of arterial pressure and the elasticity of arterial walls, but on the compensatory efficiency of shifts in blood pooling in the cranial cavity due to the release of CSF into the spinal cavity; the leading /11
role then is not played by the pulsed flow of CSF in this process as such, but rather by the interaction of pressures in the cranial and spinal cavities.

Actually, the deviation of the systolic increase of pressure in cerebral arteries is not great, and therefore only a small portion of the pulsed volume of blood reaching the cranial cavity (nearly 20 percent according to Weise, 1955) is compensated by CSF flow into the spinal cavity; the remaining volume is compensated by venous return from the cranium. However, the systolic increase of intracranial pressure gives rise to the pressure wave, which is propagated along the spinal column to its lumbar level, reflected there, and returned to the cranium, which imparts an effect on the form of the intracranial pulse curve. This wave process was studied in detail by Becher (1922) who showed that the pulse pressure wave is propagated along the spinal cavity at a rate of nearly 4 m/sec and is the reason for lumbar pulse. Bering (1955) confirmed Becher's view relative to the cranial origin of lumbar pulse by establishing that in subjects with noncommunicating hydrocephalus, the lumbar pulse is absent. To further support this point of view, our data show a significant delay (about 0.17 sec in a dog) in the pulse increase of lumbar pressure compared to the pulse increase of intracranial pressure.

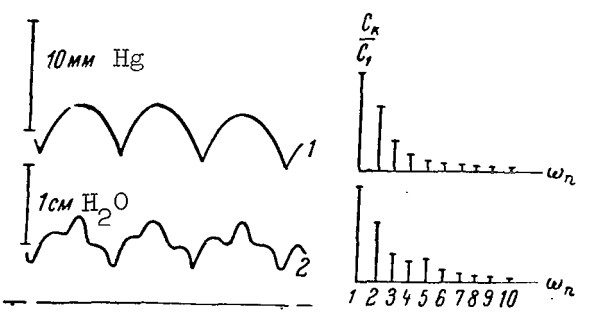

Figure 51. Pulse waves (a) of the pressure in cranial arteries (1) and intracranial pressure (2) in a dog and their harmonic makeup (b). Acute experiment. W_n: ordinal number of harmonics; $\frac{S_K}{S_1}$: ratio of the amplitude of K-th harmonic to the amplitude of the first one.

Therefore, the complex form of the pulse curve of intracranial pressure compared to the curve form of arterial pulse in cerebral vessels is due to the interaction of pressure in the cranial and spinal cavities as per the diagram in figure 25.

Therefore, the complex form of the pulse curve of intracranial pressure compared to the curve form of arterial pulse in cerebral vessels is due to the interaction of pressure in the cranial and spinal cavities as per the diagram in figure 25.

This confirms the results of an investigation of a model of intracranial circulation which we considered earlier. The curves of "pulse" waves of "intracranial" and "lumbar" pressure, recorded at the outlet of this model when fluctuations which corresponded in form to pulse pressure waves in cerebral vessels were introduced to it (fig. 52), were similar in form to curves obtainable in experiments on animals (fig. 54). /119

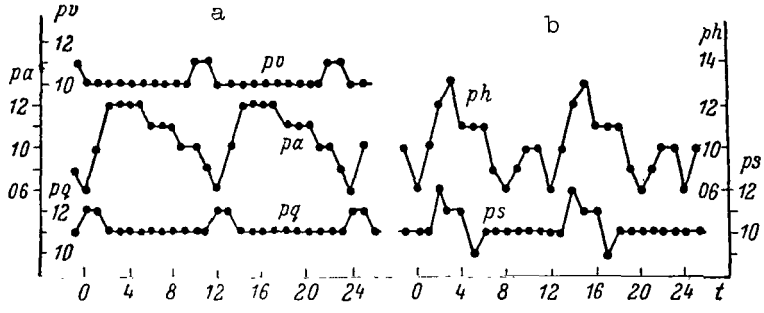

Figure 52. "Pulse" fluctuations of the input parameters of a model (a) and "pulse" fluctuations of its separate automata corresponding to intracranial (ph) and lumbar (ps) pressures (b).

pa, pv, pq are "pulse" fluctuations at inputs of the model corresponding to arterial and cranial pressures in the cranial cavity and venous pressure in the spinal cavity; pa, ph, pq, ps, pv were assigned discrete values in an octonary system of calculation where the pulse cycle was divided into 12 time intervals.

Moreover, as the experiment (in which the intracranial circulatory system was modeled) demonstrated, the resilient deformation of elastic elements of the cranium affects the form of pulse waves of intracranial pressure. This can result in the complication of pulsation form during the increase in the mean level of intracranial pressure or during impedance of the flow of blood from the cranial cavity.

The variability of fluid-pulse parameters relative to the measurement locus of pressure fluctuations and the individual features of the experimental specimens used requires special consideration. As concerns the dependence of the parameters of recordable curves on the measurement locus, its existence is conditioned by the propagation rate of the wave process in cerebral fluid spaces; all cerebral fluid spaces, as is known, form a single system, separated of course into a multitude of intercommunicating sections.

Therefore, a measurement of the propagation rate of pulse fluctuations of intracranial pressure was conducted in the hermetic cavity of the cranium (Naumenko et al., 1962; Moskalenko and Naumenko, 1964) by simultaneously recording fluctuations of pressure in central and peripheral segments of the carotid artery, intracranial pressure, and pressure in the longitudinal sinus using piezomanometers. An observable time shift of analogous pulsation phases, upon comparison of the pulsation curves of these pressures, indicates that the transmission of the pulse wave from the base of the skull to the longitudinal sinus occurs substantially faster than along a segment of carotid artery of the same length (fig. 53). Table 6 gives data on the propagation rates of pulse waves in the cranial cavity obtained by measuring the time intervals between the first moments of pressure increase in piezograms. It can be seen that the propagation rate of pulse waves in the cranial cavity is fairly high. This indicates that a difference in the form of CSF pressure fluctuations recordable in various regions of the cranial cavity must be insignificant. This was confirmed by the data of Belekhova (1958, 1959).

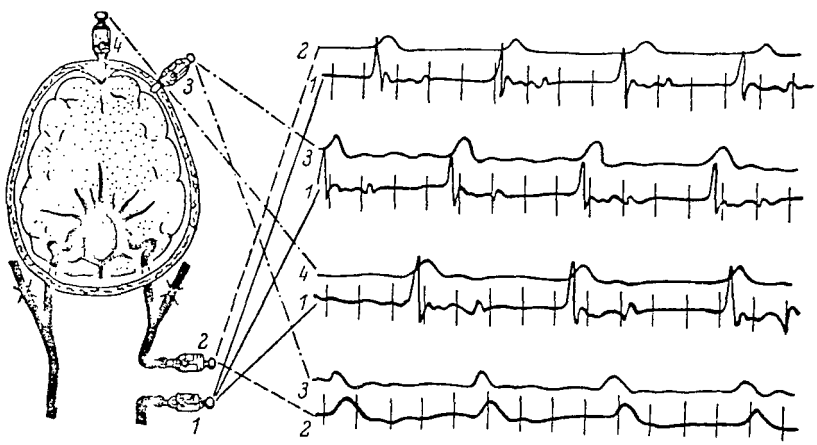

Figure 53. Diagram of the placement of pressure sensors and the curves obtained during the paired combination of various sensors which permitted calculation of pulse wave propagation rate in the closed cranial cavity.

Acute experiment on a dog. 1-4: number of the sensors; duration: 0.1 sec.

The observable variations in the form of pulse fluctuations in various experiments included, to a greater or lesser degree, occasional spikes on the intracranial pulse curve. This variability could be explained by changes in the relationship between mechanisms of the compensation of pulse increases in /120
cranial blood pooling and the nonuniform elasticity of its elastic components, which depend on the individual features of the structure of the intracranial circulatory system in various animals.

As we noted above, pulse fluctuations in intracranial pressure cause a compensatory flow of venous blood away from the cranium. Therefore, we will consider this process in the next section.

TABLE 6. PULSE WAVE PROPAGATION RATE IN THE CRANIAL CAVITY (FROM 10 MEASUREMENTS)

Sensor combination	Mean distance between sensors (cm)	Mean pulse-wave shift time (sec)	Mean wave-propagation rate (cm/sec)
1-2	5.9	0.0075	790.0
1-3	5.1	0.0019	2680.0
1-4	5.0	0.0021	2380.0
3-4	1.5	0.0006	2500.0

Note: Disposition of sensors shown in figure 53.

Section 3. Features of the Venous Flow of Blood From the Cranium

As already indicated, the pulsating nature of venous flow from the brain /121
was established long ago (Berthold, 1869; Cramer, 1873; Mosso, 1881; Keller, 1939; and others). In our own investigations, we also recorded the pulsation of blood in the cerebral longitudinal (sagittal) sinus (fig. 26) and, having compared CSF pressure fluctuation spectra in the cranial cavity and venous sinus, we established that the latter is distinguished by a somewhat lower composition of high-frequency harmonics which, as already shown, permits finding the limits of the rate of compensation of blood pooling changes in the cranial cavity as a function of venous flow. The amplitude of pulse fluctuations of venous blood pressure in the system of sinuses was close (according to our own data and those of Belekhova, 1958) to the amplitude of CSF pressure fluctuations in the subarachnoid space and fell within the limits of 2-8 mm H_2O.

The amplitude of pulse fluctuations in the jugular vein under normal conditions was extremely small and occasionally could not be recorded because of the insufficient sensitivity of the pressure sensors. However, when venous flow from the cranium was impeded by the action of negative accelerations, pulse fluctuations of venous pressure in a peripheral section of the jugular veins were recorded with sufficient clarity (fig. 64).

Considering the existence of pulse fluctuations of pressure in arteries at the base of the brain, CSF pressure, venous pressure and at the same time the evenness and the simultaneous uniformity of blood flow in the cerebral arterioles and capillaries, it is fair to conclude that pulse fluctuations in the arterial system of the brain are transmitted to the venous system via the CSF, by-passing the deep-lying cerebral vessels. The validity of this assumption concerning

the tranmission of pulsed fluctuations in accordance with the "artery-fluid-vein" system is borne out by our data on high rate of transmission of the arterial pressure pulse wave to the cerebral venous system (table 6).

The insignificant difference between the amplitude of pulse fluctuations of intracranial and venous pressure indicates that the transmission coefficient of pulse fluctuations of CSF pressure to venous blood is close to 1. In our opinion, this factor is extremely important in that it aids in revealing one of the mechanisms facilitating the high intensity of cerebral circulation. Under normal conditions, the energy of mean arterial pressure affects the movement of blood through the vascular system right down to its venous level, since the mean blood pressure in the venous system is extremely low and obviously insufficient for maintaining blood flow in the cerebral venous system. However, /122
the energy of pulse pressure fluctuations facilitates the evacuation of blood from the cranium.

The utilization of the energy of pulse pressure fluctuations for venous return from the cranium points out some peculiarities of the morphological structure of the cerebral vascular system. One of these is that a portion of the internal carotid artery (regardless of whether or not it is bent in the form of a siphon) comes into direct contact with the sinus cavernosa. Because of this, the contact serves to amplify pulsed accelerations of blood flow in veins leaving the cranium. This assumption, which was confirmed by the X-ray studies by Kopulov (1947), leads to the notion that the physiological significance of siphons of the internal carotid artery is possible, considering that an increase in the efficiency of transmission of pulsation from the arterial to the venous system depends on the contact area of arterial and venous trunks.

A similar point of view is held by Barnett and Marsden (1961) to the effect that the influence of the pulsation of internal carotid arteries on the pulsation of venous return from the cranium is more efficient when arterial blood reaches the cranium in the form of a network of vessels called the "carotid rete mirabile." The data of Baldwin and Bell (1963) also agree with this view, demonstrating that in herbivorous animals such as sheep and cattle, which are chronically in a "head down" position, the carotid rete mirabile is most strongly developed.

All of this implies that intracranial pulsation plays a substantial role in maintaining a normal level of cerebral blood flow.

Section 4. General and Local Changes in Blood Pooling in the Cranial Cavity

Pulse fluctuations of blood pressure in the cerebral vascular system and fluctuations of intracranial pressure, which were discussed in previous sections, occur in an elastic system. This must inevitably result in pulse variations in the blood volume of the cranial cavity.

Pulse variations of blood pooling in the cranial cavity can be recorded electroplethysmographically. Kedrov and Naumenko (1954) presented the first

detailed treatise on pulse waves of the intracranial EPG recorded at a frequency of about 280 kHz in acute experiments on cats and dogs.

In more recent investigations, conducted after the perfection of methods of intracranial electroplethysmography (Moskalenko and Naumenko, 1957 and 1964), the data of Kedrov and Naumenko (1954) have been confirmed many times. However, /123 a difference was observed between the volumetric intracranial pulse (recorded at low frequencies of 25-40 kHz) and complex volumetrically rapid pulse changes observed by Kedrov and Naumenko at a frequency of 280 kHz.

In recent years, two modifications of intracranial electroplethysmography permit recording from two electrodes placed on the skin of the head--rheoencephalography (Kaindl et. al., 1958; Konovalova et al., 1961; Jenkner, 1962; Veyn and Ronkin, 1962; Seipel et al., 1964; and others)--and high-frequency electroplethysmography (Beer et al., 1956; Moskalenko, 1958) used to obtain data on features of pulse variations of blood volume in the human cranial cavity. Another development has been the recording of pulse variations in the human intracranial EPG using electrodes implanted in the cranial cavity, i.e., the same methodological approaches used in animal experiments (Moskalenko et al., 1964b; Cooper et al., 1964).

Data obtained from these investigations indicate that the parameters of pulse variations in blood pooling in the cranial cavity vary strongly; this is especially true of their form. On one hand, the variability is associated with differences in the features of intracranial circulation in various biological specimens, which of itself would determine variations in the relationship between mechanisms of the compensation of volumetric changes in the cranial cavity. On the other hand, such variability can be explained by the existence of defects which vary as a function of different methods used for recording the intracranial EPGs.

The presence of the second factor confirms the position that, despite the fact that curves of the volumetric cerebral pulse presented in a number of publications by one investigator are close to one another, in comparision with the data of other investigators, occasional substantial differences are noted. Various authors have used equipment differing in frequency characteristics which would undoubtedly result in the variation of spectra of the recorded curves. For instance, the device used by Kedrov and Naumenko (1954), a mirror galvanometer, limited the capacity of obtaining high-frequency components of the spectrum of pulse variations, while devices used to record rheoencephalograms limit this capacity relative to low-frequency components, as a rule. An important cause of the occurence of varied parameters of blood pooling pulse fluctuations in the cranial cavity is the nonuniform disposition and design of electrodes used for recording the EPG; this would affect the distribution of electric current in the hermetic cavity of the cranium, and consequently, the boundaries of the investigated portion of the cranial cavity.

Considering these positions relative to factors determining the variability /124 of pulse fluctuations of blood pooling in the cranial cavity, in analyzing these fluctuations we will consider only those experimental data where the error is at a minimum, namely, data obtained using low-frequency electroplethysmographs

(0-100 Hz). We will also limit our consideration of data to variations of electrode disposition that yield the most complete information. In general, we will consider the following volumetric variations in blood pooling in the cranial cavity.

1) Total changes in the blood pooling of the cranial cavity observable during the bitemporal insertion of electrodes into the cranial cavity of animals under acute and chronic experimental conditions. Similar changes in blood pooling in the human cranial cavity are observed using contactless, high-frequency electroplethysmography and when electrodes are placed on skin close to natural cranial openings.

2) Local changes in blood pooling in individual vessels of the pia mater observable during the relatively close positioning of electrodes in contact with the dura mater.

3) Local changes in the blood pooling of deep portions of the brain observable when using electrodes implanted in the cerebral matter.

In each variation of electrode disposition we obtained relatively similar data. In each case, the variability of obtainable curves was not greater than during the recording of pulse fluctuations of intracranial pressure.

The similarity of the curves of the intracranial EPG during the enumerated variations of electrode disposition once again convinced us that electroplethysmography, notwithstanding its inherent error, can yield reliable information on pulse variations of blood volume in the closed cranial cavity. However, considering the variability of EPG pulse wave parameters, it is necessary to analyze intracranial EPG pulse waves with extreme caution.

We will now consider the experimental data.

The total pulse variations in cranial blood pooling are distinguished by comparatively small values. The amplitude of pulse waves in large laboratory animals ranges from 0.01 to 0.05 percent of the general electroconductivity between electrodes.

Typical pulse fluctuations of total blood pooling in the cranial cavity are /125
shown in figure 54. As is evident, pulse waves of total blood pooling in the cranial cavity are complex in form and consist of three peaks (fig. 54,2) reminiscent of pulse fluctuations of intracranial pressure (fig. 54,3). The relative magnitudes of these peaks vary in different experiments.

In bringing attention to the occurrence of small shifts of CSF between the cranial and spinal cavities and also to the interaction of pressure between these two cavities, it is to be expected that pulse fluctuations of total blood pooling in the cranial cavity corresponds to pulse variations of CSF in the spinal column. To confirm as well as reveal whether shifting of CSF between the cranial and spinal cavities is the only reason for pulse variations of total blood pooling in the cranial cavity, we simultaneously recorded pulse variations of the cerebrospinal EPG and CSF pressure in the cranial cavity and at the

the lumbar level of the spinal cavity. The results of these tests are shown in figures 54, 4, and 5. From the curves of the intracranial and cerebrospinal EPGs, it is evident that the initial value of the total blood volume in the cranial cavity (fig. 54, curve 3, section ab) is a function of the flow of CSF into the spinal cavity, since the increase in blood pooling in the cranial cavity corresponds to a simultaneous rise in blood pooling in the spinal column. This indicates the presence of other volumetric reserves in the cranial cavity which were mentioned earlier (p.82).

The second wave of the increase in total cranial blood pooling (fig. 54, curve 3, section bd) corresponds to a decrease in blood pooling of the cerebrospinal cavity which indicates sufficiently well the flow of some CSF into the spinal cavity and constituting 20 percent of the pulse volume of blood arriving at the cranial cavity.

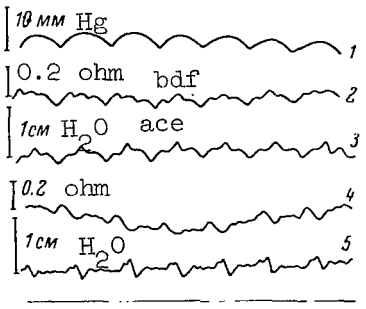

Figure 54. Pulse pressure waves in cranial arteries (1), the intracranial EPG (2), intracranial pressure (3), the cerebrospinal EPG (4), and CSF pressure at the lumbar juncture of the spinal column (5).
Acute experiment on dog. Duration: 1 sec. Remaining explanations in the text. 1. 10 mm Hg; 2. 0.2 ohm (abcdef); 3. 1 cm H_2O; 4. 0.2 ohm; 5. 1 cm H_2O.

After the second rise in the intracranial EPG, there is a third one (fig. 54, curve 3, section df). Thus far, it is difficult to explain what forces /126
are responsible for this increase in cranial blood pooling during a decrease in the dicrotic arterial pulse wave. However, having considered Becher's view (1922) on the presence of a pressure wave developing in the cranium at the beginning of the cardiac cycle and propagating along the spinal column, the origin of the third wave and the intracranial pulse can be attributed to the return of the CSF pressure wave to the cranium after its reflection from the lumbar level of the spinal column. It is not impossible that this wave generates an oscillatory process in the spinal column which in turn causes the second as well as the third wave of the intracranial pulse. These hypotheses require special checking.

It is entirely possible that an essential role is played by the brief increase in venous pressure which occurs as a result of the closing of atrial valves in the genesis of the EPG pulse wave as well as intracranial pressure, as noted in the work of Sicutery (1959).

Despite the fact that all these factors causing pulse fluctuations of total blood pooling in the cranial cavity are as yet unclear, the data we have considered permit the conclusion that the compensation of pulse fluctuations of total blood pooling in the cranial cavity are effected by two modes: first, via a shift in CSF between the cranial and spinal cavities, and second, by virtue of the distension of elastic elements of the cranial cavity. However, the latter mode probably plays a secondary role.

Thus far, we have only considered data obtained by investigating higher vertebrates and man. However, electroplethysmography can also be applied to evaluating pulse fluctuations of total cerebral blood pooling in lower vertebrates. Therefore, in cooperation with D. I. Pesennikova and A. A. Shurubura, we used this method to reveal some features of the parameters of changes in blood pooling in some representatives of the lower vertebrates.

Such investigations are of special interest for comprehending the phylogenetic development of intracranial circulatory systems. Our knowledge of this area is thus far limited to data on the morphological features of arterial trunks supplying blood to the brain (Naumov, 1951; Klosovskiy, 1951) and variations of the structure of the circle of Willis and basic cerebral arteries (Critchley, 1930; Craigie, 1945; Gindtse, 1947; Izmaylova, 1957).

Problems of the comparative physiology of this system have absolutely not been considered. Only two works (Berezin, 1916; Sakhnovskaya, 1919) are known concerning a comparative analysis of the reactions of the cerebral vessels of the pike and rabbit to some pharmacological agents. /127

Our investigations, conducted on three classes of vertebrates (amphibia--frogs; reptiles--turtles (Emys obicularis) and lizards (Varanidae) birds--pigeons and chickens), together with data obtained from mammals (rats, rabbits, cats, dogs) and human subjects, indicate that the amplitude and form of pulse waves of the intracranial EPG vary uniformly as a function of the progression from one class of animals to another.

Progressing up the evolutionary tree, the organization of pulse fluctuations of total blood volume in the cranium increases, reaching its highest values in mammals (table 7). These uniform changes assume the form of pulse waves. If in frogs and turtles pulse fluctuations of the intracranial EPG assume the form of one wave, in the lizard there is an additional peak on the pulse curve (fig. 55). The intracranial pulse in mammals, including man (fig. 56), is more complex in form when compared to these animals.

It is absolute that a difference in the parameters of intracranial pulsation in various representatives of the vertebrates is due to a certain degree of /128 variation in the relative magnitude and form of pulse variations of arterial pressure. However, the differences in the latter are obviously not significant enough to explain the peculiarities of the form of total cranial blood pooling curves for various classes of vertebrates since EPG pulse waves of the rear extremities of the species enumerated above, for instance, were quite dissimilar.

It is possible that the observable complication of pulse waves of changes in cranial blood pooling in a number of vertebrates is the result of the refinement of mechanisms compensating changes in the volume of cranial blood due to an intensification of cerebral blood flow.

TABLE 7. AMPLITUDE OF EPG PULSE WAVES IN VARIOUS ANIMALS AND MAN

Animal	No. of specimens	Relative pulse variation of electrical conductivity in the cranial cavity (percent of mean value of electrical conductivity)
frog	7	0.005±0.002
turtle	8	0.007±0.003
lizard	12	0.010±0.002
pigeon	8	0.012±0.006
chicken	7	0.012±0.005
rat	15	0.015±0.005
rabbit	18	0.017±0.008
cat	12	0.020±0.010
dog	10	0.030±0.020
man	6	0.050±0.030

Human EPG measured with subdurally implanted electrodes.

In a number of animals studied by us, the form of pulse waves in the intracranial EPG depends on features of the structure and activity of the heart. For instance, in rats, which are distinguished by a high heart rate, characteristic peaks on the curves of pulse waves of the intracranial EPG were more weakly expressed than in other mammals. This peculiarity of intracranial volumetric pulsation in rats in all likelihood is due to the fact that at a high cerebral beat frequency, CSF does not have a chance to flow into the spinal cavity during the cardiac cycle as opposed to other animals with a substantially lower cerebral pulse frequency.

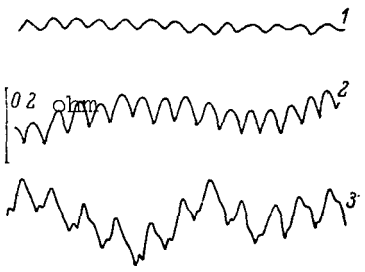

Figure 55. Pulse waves of the intracranial EPG in the frog (1), turtle (2), and lizard (3). Duration: 1 sec

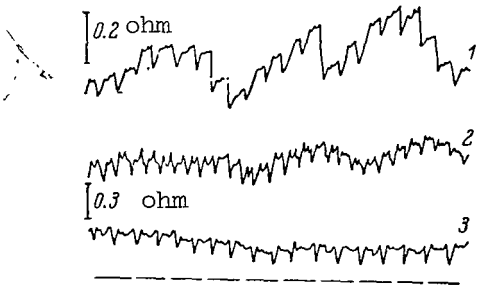

Figure 56. Pulse waves of the intracranial EPG for the pigeon (1), dog (2), and man (3). Duration: 1 sec

In birds, also distinguished by a high heart rate, the form of intracranial EPG pulse waves is also substantially smoothed. However, in birds this might be due to the lack of CSF (Fridman, 1957) which apparently alters the very compensatory mechanism of changes in cranial blood pooling. However, this proposition requires special confirmation.

The data considered on features of pulse changes in cranial blood pooling in representatives of some vertebrate classes sheds light on only a few characteristic tendencies in changes of parameters of pulse waves of the intracranial EPG in a number of vertebrates. These results can be considered only as the initial stage of investigations in this direction. They perhaps introduce more new questions than they do answers to the one originally put forward. However, we presented these data to bring the attention of researchers to an important and interesting problem, the study of which is now possible thanks to the creation of new methods of investigating the intracranial circulatory system. /129

We will now turn to local changes in cranial blood pooling. As was mentioned earlier (p. 100), the basic portion of the pulse dilation of the cerebral arterial system is compensated by the flow of venous blood from the cranium; in other words, there is an interconnected change in volumes occupied by arterial and venous blood in the cranial cavity. Considering the features of the morphology of the cerebral vascular system, it can be expected that the distribution of blood volume in the cranial cavity must take place fundamentally between arteries based in the cranium and veins based in the formix, although many large veins are also located at the base of the cranium. To confirm the actual existence of such a transdistribution of cranial blood pooling, during a number of variations in the positioning of electrodes at various distances from the base of the cranium (fig. 57), when electrodes were placed close to the base of the cranium there was an increase in impedance during the systole; this indicates an increase in blood pooling in this area. When electrodes were placed near the arc of the cranium, there was a decrease in impedance indicating a decrease in blood pooling. Curves of pulse waves of the intracranial EPG recorded as in the above cases were uniformly phased; here a change in blood pooling occurred in the first half of the cardiac cycle. When electrodes occupied an intermediate position in recording an EPG, a steady change in the direction of the pulse wave was noted (fig. 57). These experiments indicate that there is a shift in the distribution of arterial and venous blood volumes in the cranium at the moment of the basic inflow of blood.

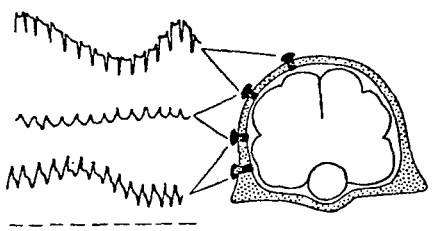

Figure 57. Pulse waves of the intracranial EPG in a dog recorded during various electrode dispositions. Acute experiment, duration: 1 sec

Local pulse changes in cranial blood pooling were also noted when the EPG was recorded from electrodes implanted in cerebral tissue. Like data were obtained from human subjects when EPGs were recorded from tens of gold electrodes implanted in deep sections of the brain for therapeutic purposes (Moskalenko et al., 1964; Cooper et al., 1964). /130

The parameters of pulse fluctuations of blood pooling in deep sections of the brain differ substantially from earlier noted parameters of pulse fluctuations of the intracranial EPG recorded from surface electrodes. The EPG readout from various combinations of implanted electrodes showed that the nature of blood pooling pulsation in deep sections of the brain depends little on the positioning of electrodes. The parameters of curves obtained when electrodes were placed in various levels of the white and gray matter were extremely close to one another.[1]

Local pulse changes in the blood pooling in deep sections of the brain are distinguished by extremely variable amplitude. Their magnitude significantly varies not only during the action of some factors, but even in a quiet, supine human subject (fig. 58). In a number of cases we observed that the direction of pulse waves in deep sections of the brain can reverse without any apparent reason both under normal conditions and during the action of some factors (fig. 58). The variability of the amplitude of EPG pulse waves in deep sections of the brain was also observed in curves obtained by Kedrov and Naumenko (1954) when recording an EPG from electrodes implanted in the cerebral tissue of animals.

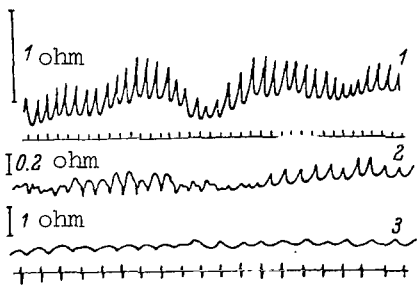

Figure 58. Pulse waves of an intracranial EPG in a quiet, supine human subject recorded from electrodes 2.5 cm apart located in the white matter of the brain. 1, 3 under normal conditions (recorded at various rates and amplifications); 2. exposure to CO_2. Duration: 1 sec

Pulse waves of blood pooling in deep sections of the brain, as evident in figure 58, are substantially smoothed compared to blood pooling in surface areas. Pulse waves of similar form were also recorded by Kedrov and Naumenko (1954). What do pulse fluctuations in deep sections of the brain represent? /131

Volumetric reserves of deep sections of the brain are extremely limited but exist nonetheless. According to Sepp (1928), pulse variations in cerebral blood pooling can occur as a function of the flow of CSF from perivasuclar fissures or spaces of Virchow-Robin adjacent to deep vessels. We feel that this possiblity is sufficiently realistic since the existence of perivasucular fissures has been demonstrated in a number of morphological investigations (Ranson and Clark, 1953; Zavarzin and Schelkunov, 1955; Shamburov, 1954; Bowsher, 1957 and others).[2] Some authors such as Sepp (1928) underlined the great significance of these spaces as absorbers of pulse fluctuations of pressure (Pedrazzini, 1938).

[1] It should be observed that observations were conducted only in cases when electrodes were implanted in the frontal area of the brain.

[2] A question open for discussion here is whether these fissures (or spaces) are continous channels or whether they are interrupted at the capillary level.

Furthermore, it is not impossible that the dilation of deep arteries is associated with the construction of veins situated in that same cerebral area.

In our opinion, the limited nature of volumetric reserves in deep sections of the brain were over-categorized by Kedrov and Naumenko (1954), who concluded that pulsation in these cerebral areas is reflected only by fluctuations in blood flow rate in the absence of changes in the volume of circulating blood. To support this point of view, these authors allude to the fact that, according to their data from a study using an ac current (about 280 kHz) for electroplethysmography, changes in blood flow rate are recorded. As demonstrated in Chapter I, in this electroplethysmographic frequency range changes in blood flow rate are, in fact, primarily recorded. However, it is difficult to reconcile ourselves with the point of view of Kedrov and Naumenko since, in an elastic system, each change in the blood flow rate must correspond to a change in blood pressure and the latter of necessity must result in a change in the volume of deep vessels.

The curves shown in figure 58 illustrate the presence of the volumetric pulse in deep vessels. Contrary to the experiments of Kedrov and Naumenko, the EPG was recorded at low frequencies in this case, such that changes in electrical conductivity reflect changes in blood pooling. Nonetheless, the changes in blood flow rate associated with cardiac activity and observed in the experiments of Kedrov and Naumenko (1954) absolutely do exist.

Having acknowledged the existence of pulsations of blood volume and blood flow rate in the vessels of deep cerebral areas, we must recall earlier-mentioned contradictions to this point of view (p. 92) reflected by data on the absence of cerebral pulsation. /132

In our view, the contradictions of two categories of data, i.e., the presence of pulsation in the closed cranial cavity on one hand and its absence in arteries and capillaries on the other, are only superficially apparent and are due to the low sensitivity of experimental methods. Data obtained by Klosovskiy support our notion of the features of intracranial pulsation indicating that the considered processes completely absorb pulse fluctuations of pressure on the arteriole and capillary level, although they have not yet been observed.

Section 5. Changes in the Parameters of Pulse Fluctuations of the Intracranial EPG and Intracranial Pressure During Accelerations

As shown in the previous sections, the characteristics of pulse fluctuations of intracranial pressure and blood pooling in the cerebral vascular system, their amplitude and their form under various conditions depend on the elastic nature of the vascular network and, in particular, on the tonus of cerebral vessels and the efficiency of compensatory mechanisms of changes in cranial blood pooling.

Therefore, investigations of the dynamics of parameters of intracranial pulsation during the action of various factors can be of substantial interest in comprehending the character of changes in intracranial circulation.

However, up to the present time, questions of changes in pulsation parameters in the closed cranial cavity during exposure to various physical factors have received little attention. Only data on changes in the amplitude of pulse fluctuations of intracranial pressure are known (Falkenheim and Naunyn, 1887; Becher, 1922; Nadzharyan, 1958; Rider et al., 1952; Belekhova, 1958; Naumenko and Vasilevskiy, 1962) as well as the amplitude of pulse waves of the intracranial EPG and the rate of venous flow from the cranium (Kedrov and Naumenko, 1954). There are also data on changes in intracranial pulsation recorded by rheoencephalography during various pathological conditions (Seipel et al., 1962; Jenkner, 1964; Yarullin, 1965; and others).

Recently, the results of our investigations were published concerning changes in intracranial pulsation during the action of low-magnitude longitudinal accelerations (Moskalenko et al., 1962, 1964a, 1964b; Cooper et al., 1964).

In this section, we will systematically present the data from these publications, having supplemented them with new experimental material which we obtained during the action of longitudinal and transverse accelerations as well as during the action of other factors. /133

We will analyze experimental data on the dynamics of the parameters of pulse fluctuations of blood pooling and intracranial pressure during accelerations. However, we will first consider how (if we proceed from figure 25) some more elementary factors, influencing only some individual links of this picture while leaving the remainder unchanged, affect this dynamic process. This permits revealing more completely the problem of the mechanisms of changes in intracranial pulsation.

During increased venous pressure in the cerebral vascular system caused by the impedance of venous return from the cranium, pulse waves of the intracranial EPG must also increase, since the compensation of changes in blood pooling in the cranial cavity via venous flow from the cranium is inhibited in this case and the magnitude of the compensatory flow of CSF into the spinal cavity increases. The latter must also lead to a complication of the form of pulse waves (p.101). Actually, in acute experiments on animals (dogs and cats) we observed that during the occlusion of both jugular veins, pulse waves on the curve of the intracranial EPG increased somewhat and that their form was more complex (fig. 59,2).

During the impedance of venous flow from the cranium occurring simultaneously with an increase in the amplitude of pulse waves of the intracranial EPG, an increase in the amplitude of intracranial pressure pulsation is to be expected, which is also confirmed by experimental data (fig. 59,1).

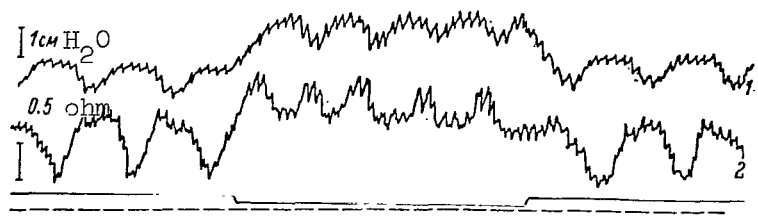

Figure 59. Change in the pulse waves of the intracranial EPG (1) and intracranial pressure (2) in cats during occlusion of both jugular veins. Acute experiment. Duration: 1 sec

The increase in intracranial pressure must correspond to an increase in the amplitude of its pulsation since during increased intracranial pressure, the transmission of arterial pulsation of the CSF is facilitated.

Actually, Ryder et al. (1952) demonstrated that during an increase in the /134
volume of CSF in the cranial cavity inducable by an injection of a physiological solution (Riuger's solution) into the subarachnoid space, pulse fluctuations of intracranial pressure increase. McQueen and Jeanes (1964), in studying the role of increased fluid pressure caused by the inflation of a rubber bulb inserted into the cranial cavity, made it a special point to stress that during hypertension, pulse waves of intracranial pressure increase.

We also observed an increase in the amplitude of pulse waves of intracranial pressure and cranial blood pooling in an acute experiment conducted on cats during increased intracranial pressure caused by pressure applied to the abdomen (fig. 29).

Therefore, regardless of the method, during increased intracranial pressure the amplitude of its pulse oscillations increases.

A change in the tonus of arterial vessels must substantially affect the parameters of pulse waves of intracranial pressure and the intracranial EPG, since under this condition the coefficient of transmission of pulse pressure waves to the CSF changes. For instance, a decrease in the tonus of cerebral arteries alleviates the transmission of pulse fluctuations of blood pressure to the CSF, which results in an increase in the amplitude of pulsation of both the intracranial EPG and intracranial pressure.

This is confirmed by experimental data. Naumenko and Vasilevskiy (1962) recorded an increase in the amplitude of pulse fluctuations of intracranial pressure while Kedrov and Naumenko (1954) observed an increase of pulse fluctuations in the intracranial EPG and drops in the rate of venous flow during a sharp decrease in the tonus of cerebral vessels caused by CO_2 respiration. An increase

in the amplitude of intracranial pulsation during vasodilatory reactions was observed by Bekhterev and Myasishchev (1928).

We observed a 2- to 3-fold increase in pulse fluctuations of cranial blood pooling during the vasodilatory reaction of intracranial vessels dircetly after the action of accelerations, which caused the blood to flow away from the head. As shown in figure 60, the substantial changes assume the very form of pulse fluctuations.

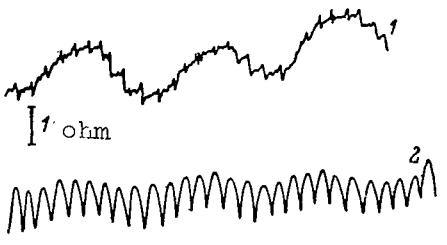

Figure 60. Change in pulse waves of the intracranial EPG in the cat during the decreased tonus of intracranial vessels after exposure to a positive acceleration of 1 G*. Acute experiment. 1. before acceleration; 2. after acceleration. Duration: 2 sec

The indicated data, showing results of one or another factor on parameters of intracranial pressure, encompass only a small portion of the factors experienced by the organism under normal conditions.

During accelerations, the dynamics of parameters of pulse fluctuations of blood pooling and intracranial pressure are determined by a number of passive and active factors. The first, as we have already indicated, is a change in venous flow from the cranial cavity and conditions of the compensatory shift of CSF into the spinal cavity; the second is the specific reactions of the cerebral vascular system and other cardiovascular systems to such a factor. /135

In consideration of the basic factors determining the parameters of intracranial pulsation during longitudinal accelerations, we simultaneously recorded pulse fluctuations of the intracranial EPG, intracranial pressure, the level of blood pooling in the cranial cavity, and CSF pressure. This permitted revealing the moment of inclusion of active reactions of the cerebral vascular system during the action of the stimulus.

One additional factor, whose possible influence on parameters of intracranial pulsation should be considered, is a change in cardiac activity developing as a result of longitudinal accelerations. However, a fairly extensive amount of experimental data accumulated in recent years indicates that a change in cardiac activity is extremely insignificant during the majority of experiments in which accelerations such as those in our studies (up to 1 G) are used. Browne and Fitzsimons (1959) demonstrated that noticeable changes in human heart rate occur during exposure to positive accelerations starting at 1.5- 2.0 G. According to Lindberg et al. (1960), arterial pressure varies by 9 percent and

*1 G= the magnitude of the longitudinal vector.

minute cardiac volume by 7 percent in the dog during exposure to positive accelerations of about 2 G. Similar data are also to be found in the works of Hershgold (1960) and Shanker (1963). Nevertheless, in many cases, observations of arterial pressure were made as a control of cardiac activity.

In the absence of active reactions of the cerebral vascular system during /136
relatively small negative accelerations, an influx of blood to the cranial cavity is associated with an increase in the amplitude of pulse fluctuations of intracranial pressure by 15-20 percent and a significant complication of the form of pulsation curves. During positive accelerations, a change in the form of pulse fluctuations of intracranial pressure assumes a contradictory nature and their amplitude increases by a factor of 1.5-2.0 (fig. 61). Significant changes are also experienced by pulse fluctuations of total blood pooling in the cranial cavity. During negative accelerations, the amplitude of pulsation usually decreases somewhat and the form of the fluctuation is complicated. During positive accelerations, peaks in pulse curves of the intracranial EPG are smoothed and pulsation amplitude simultaneously increases significantly.

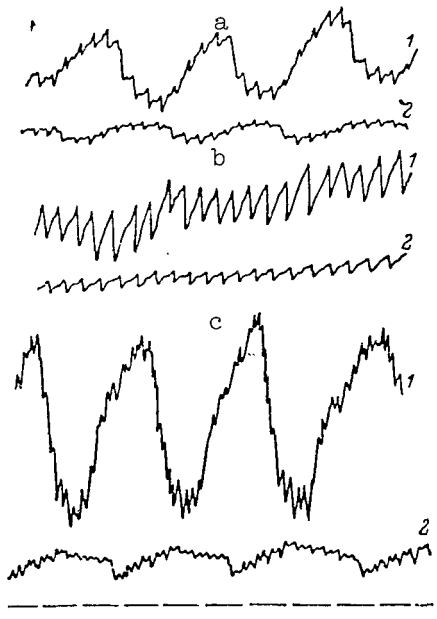

Figure 61. Changes in the pulse fluctuations of the intracranial EPG (1) and intracranial pressure (2) in a dog during low-magnitude longitudinal accelerations a. before acceleration; b. during positive acceleration; c. during negative acceleration. Duration: 1 sec

In different groups of biological specimens, the dynamics of intracranial pulsation during exposure to positive and negative accelerations are identical. Thus, we observed a complication of the form of pulse changes of cranial blood pooling in both mammals (fig. 61) and reptiles (fig. 62). The greatest changes in the parameters of intracranial pulsations were noted in cases where the spectral composition of pulse waves under normal conditions were characterized by a relatively high complement of high-frequency harmonics.

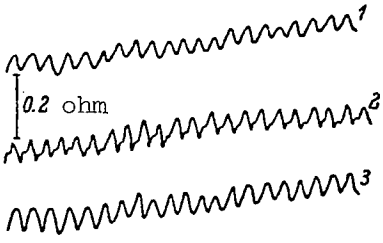

Figure 62. Change in pulse fluctuations of the intracranial EPG in the turtle during longitudinal accelerations. 1. before acceleration; 2. during a 1-G negative acceleration; 3. during a 1-G positive acceleration. Duration: 1 sec

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We observed these changes in the parameters of pulse fluctuations of blood pooling and CSF pressure in the closed cranial cavity in animals under moderate urethane anesthesia at longitudinal accelerations of up to 0.4-0.5 G and under deeper anesthesia at accelerations of up to 0.8-1 G. Such a difference in the /137 acceleration magnitude corresponds to a different threshold of inclusion of cerebral vascular reactions.

The dynamics of the amplitude of pulse fluctuations of the intracranial EPG and intracranial pressure during longitudinal accelerations within the limits outlined above can be understood if we proceed from peculiarities of the compensation of changes in blood volume in the cranial cavity. Actually, during a negative acceleration the impedance of venous flow from the cranium causes an increase in the mean level of intracranial pressure resulting in a rise in the amplitude of its pulse fluctuations, while the amplitude of pulse fluctuations of blood pooling decreases, since their compensation is rendered more complicated. A complication of the form of pulsation indicates that the significance of the second compensatory pathway of cranial blood pooling increases despite the fact that during negative accelerations the shift of CSF to the spinal cavity is also impeded. A change in the relationship between the mechanisms of compensation during positive accelerations in all likelihood leads to a simultaneous increase in pulse waves of the intracranial EPG and intracranial pressure.

The fact that there is a change in the relative role of the compensatory mechanisms of pulse increases in cranial blood pooling during accelerations is confirmed when a comparison is made of pulse changes in blood pooling in the cranial and spinal cavities during longitudinal accelerations of various magnitudes. Figure 63 shows clearly that during a negative acceleration the negative/138 phase of the pulse wave of the cerebrospinal EPG corresponding to a shift of CSF from the cranial cavity to the spinal cavity during an influx of blood to the head is more pronounced when compared to a situation caused by a positive acceleration and is less pronounced during the flow of blood away from the head.

During negative accelerations, the consequence of an increase in the mean level of pressure in the system of the vena cava superior are noticeable pulse fluctuations in the peripheral section of the jugular vein (fig. 64) which can be recorded under normal conditions. The increase of pulse fluctuations of pressure of venous blood flowing away from the brain during negative accelerations

also indicates that the compensation of pulse changes in blood pooling due to venous flow from the cranium is impeded in this case.

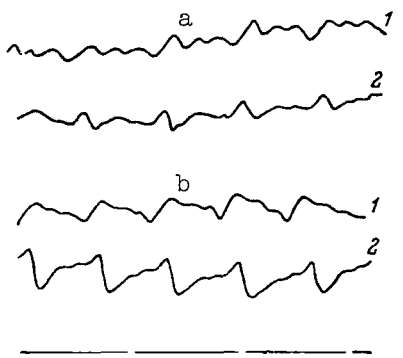

Figure 63. A change in pulse waves of the intracranial (1) and cerebrospinal (2) EPG in a dog during longitudinal accelerations. a. positive acceleration; b. negative acceleration. Duration: 1 sec

We observed substantial changes in the pulse fluctuations of the intracranial EPG and intracranial pressure during transverse accelerations. In acute experiments on dogs at accelerations of 8-10 G, there was often somewhat of an increase in the amplitude of CSF pressure fluctuations in the cranial cavity shortly after the beginning of exposure (fig. 65). Simultaneously with an increase in pulse fluctuations of intracranial pressure, there is a decrease in pulse fluctuations of cranial blood pooling. Upon a further increase in acceleration magnitude (to 15-20 G), pulse fluctuations of intracranial pressure as well as fluctuations of the intracranial EPG decrease when compared to a normal background. However, at still higher accelerations (35-40 G) pulse fluctuations of intracranial pressure substantially increase once again (fig. 65). After stopping the centrifuge, pulse waves of intracranial pressure and the intracranial EPG as a rule were significantly increased relative to their pre-exposure values.

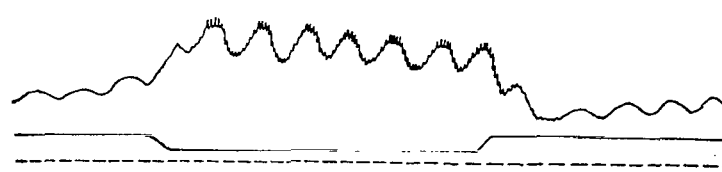

Figure 64. Change of pressure in the peripheral section of the jugular vein of the cat during a 0.8-G negative acceleration. Acute test. Duration: 1 sec

At medium acceleration magnitudes (up to 10-15 G), normalization of the amplitude of pulsation in a dog under anesthesia occurred 1-2 min after stopping the centrifuge, while at greater magnitudes (25-40 G) this process took 4-8 min.

We observed substantial changes in the amplitude of pulse fluctuations of /140
the human intracranial EPG recorded from electrodes placed on the skin of the head during transverse accelerations of 10-12 G (fig. 66). After the beginning of rotation and during a steady buildup to 2-3 G, pulse waves of the intracranial EPG did not noticeably change, but later their amplitude dropped sharply. When we stopped the centrifuge, pulse waves of the human EPG recovered to the original level during a slow-down to 2-4 G. After the centrifuge was stopped, pulse waves of the intracranial EPG often increased somewhat and their subsequent decrease to the original level was observed 3-6 min after the centrifuge was stopped.

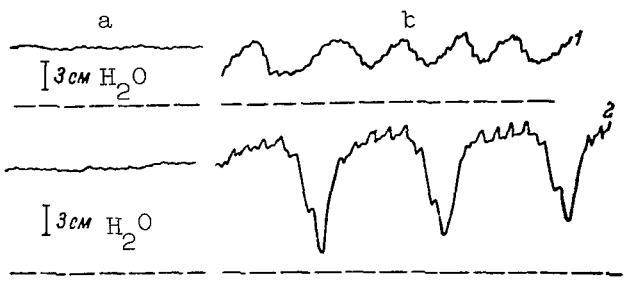

Figure 65. Pulse fluctuations of intracranial pressure in a dog under normal conditions (a) and their variation during exposure to accelerations (b). Acute experiments. 1. during a 10-G transverse acceleration; 2. during a 40-G transverse acceleration. Duration: 1 sec.

The dynamics of intracranial pulsations during transverse acclerations are apparently conditioned by a number of factors; pulmonary blood deposition and disrupted cardiac activity can be considered as some elementary mechanisms which lead to a shift in systemic arterial and venous pressure and decreased blood oxygenation (Armstrong, 1954; Kotovskaya and Yuganov, 1962; Wood et al., 1963; Hardy, 1964; Banchero et al., 1965). In its own unique fashion, this could cause a shift in the conditions of blood influx to and venous flow away from the cranium and a change in the tonus of cerebral vessels. It is not impossible that a trans-distribution of blood in the cranium is also of considerable significance in possibly leading to a disruption of blood supply to individual sections of the brain. The accompanying longitudinal component of the acceleration might also play a small role.

Data obtained during high magnitudes of acceleration require special consideration since they appear to be paradoxical; at high accelerations, the vital organs of the circulatory system are practically nonfunctional.

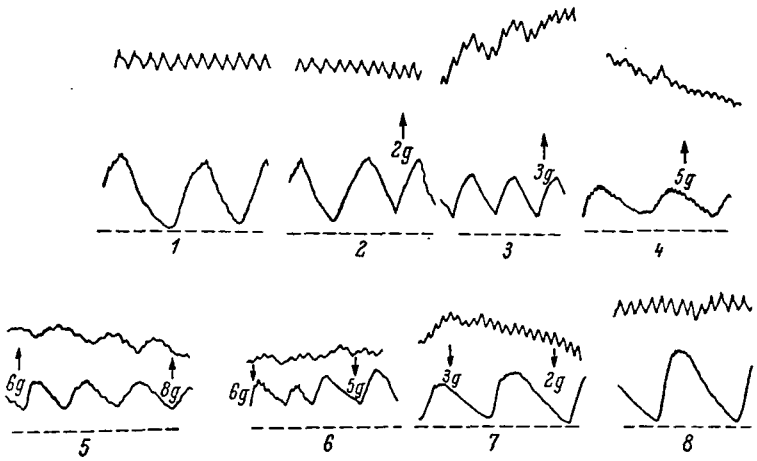

Figure 66. Change in the amplitude of pulse fluctuations of the human intracranial EPG during transverse accelerations. Electrodes placed on the skin of the head.

Upper arrows=magnitude of acceleration during buildup; arrows pointing-down=slowing-down of the centrifuge. Upper curves EPG; lower curves, respiratory movements. 1. before exposure; 2-7 during exposure; 8. 2 min after exposure.

One of the few possible explanations of this phenomenon might be based on a hypothesis of the existence of active pulse changes of tonus in intracranial vessels occurring as a result of the interaction of cerebral centers controlling cardiac activity and respiration on one hand and centers controlling cerebral vascular tonus on the other. In other words, this phenomenon agrees with the notion of Yanovskiy (1922) relative to the peripheral heart, which was subjected to serious criticism by a number of authors (Val'dman, 1961).

It is possible that under normal conditions, active pulse changes of cerebral vascular tones are masked by processes of a mechanical nature, i.e., by pulsed fluctuations of arterial pressure which render them difficult to observe. However, under very extreme conditions, during the action of high-magnitude transverse accelerations, when the heart continues to function but its delivery pressure is absent, pulse changes in the tonus of intracranial vessels become noticeable. For such an explanation to have credence, further investigations on this interesting problem must be conducted. /141

We will now consider features of the dynamics of pulse changes of blood pooling in deep sections of the brain under various conditions. Observations which we conducted on human subjects with implanted electrodes demonstrated that the amplitude of pulse fluctuations of blood pooling during exposure to various

factors decreased somewhat as a rule. Hence, the amplitude of pulse changes in the blood pooling of deep cerebral regions decreases by several times both during positive and negative accelerations, during CO_2 respiration, and during

pressure applied to the abdomen; it can change, as we demonstrated earlier (p.111) in the absence of any physical factors (fig. 67). Changes in the amplitude of pulse fluctuations of blood pooling in deep cerebral areas are accompanied by shifts in their phase which are so great that they cannot be explained by variations in the propagation rate of the pulse wave (fig. 68). The form of pulsation in all these cases does not change for all practical purposes.

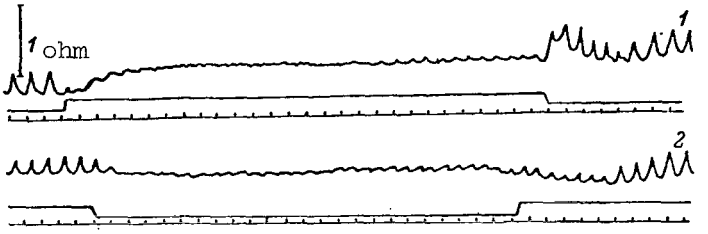

Figure 67. Dynamics of the human intracranial EPG during longitudinal accelerations. Electrodes implanted in the white matter of the brain. Distance between electrodes is 2.5 cm. 1. positive 0.5 G acceleration; 2. negative 0.5 G acceleration. Duration: 1 sec

These factors indicate that the dynamics of pulse fluctuations of blood pooling in deep cerebral areas are subordinated by mechanisms which differ from those which determine the dynamics of pulse fluctuations of intracranial pressure and total blood pooling in the cranial cavity. However, changes in the total blood pooling in the cranial cavity affect the magnitude of the pulsation of blood pooling in deep cerebral sections, causing a more-or-less significant decrease in this phenomenon in the majority of cases.

The dependence of changes in the amplitude of pulsation of blood pooling in deep cerebral sections on the level of total blood pooling in the cranial cavity can be understood, having recognized that the basic portion of the energy of systolic pressure diverges into the surface cerebral vessels. Here, the magnitude of pulse changes in blood pooling in deep vessels will depend on the difference between the energy of pulse fluctuations of blood pressure in cranial arteries and energy expended by the pulsed flow of blood and CSF from the cranial cavity. During exposure to the majority of factors, the energy expenditure for the transmission of pulse waves to the cranial cavity increases, since in some cases blood flow from the cranium is impeded while in others, to the contrary, more favorable conditions are created for efflux. Thus, during exposure to many factors, a decrease in the amplitude of pulse fluctuations of blood pooling in deep sections of the brain is observed--right down to its complete disappearance. Therefore, pulse changes in blood flow under certain

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conditions can be completely extinguished even in deep cerebral arteries, not to mention arterioles and capillaries.

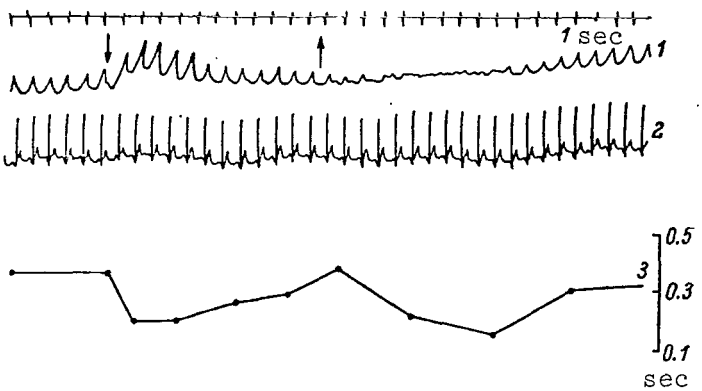

Figure 68. Change in the human intracranial EPG recorded under the same conditions as in figure 67 during pressure applied to the abdomen. 1. EPG; 2. ECG; 3. Change in the interval of time between the R wave of the cardiogram and the peak of the intracranial EPG.

Arrows show beginning and end of pressure. Duration: 1 sec

During exposure to factors wherein intracranial pressure increases but conditions for the flow of venous blood from the cranium are unaltered, pulse-wave transmission from the arterial to the venous system of the brain takes place with a smaller expenditure of energy. As is evident in figure 68, the first moments after the beginning of the factor result in a somewhat increased amplitude of pulsations.

Thus far, it is difficult to fully comprehend the reason for phase shifts /143
of pulse fluctuations of blood pooling in deep cerebral areas, especially its spasmodic 180° changes (fig. 68).

It is possible that such a phase shift is determined by compensatory conditions of blood pooling in cerebral arteries of the pia mater. Hence, for instance, if more favorable conditions for the compensation of blood pooling changes are created by the flow of venous blood from the cranium, which is observed at the beginning of the cardiac cycle, the phase shift of pulsations in deep cerebral areas must increase. If there is an improvement in conditions for the compensation of pulse changes in blood pooling in the cranial cavity by virtue of CSF flow into the spinal cavity, the phase shift must decrease. This hypothesis is confirmed to a certain degree by data on changes in the phase of human EPG pulse waves compared to ECG curves (fig. 68) during abdominal pressure. During the action of this factor, the compensatory flow of CSF into the spinal cavity is impeded as a result of increased blood pooling in the spinal sinuses,

while a compensation of changes of blood pooling in pia mater vasculature is improved as a result of increased intracranial pressure. Here, a decrease in the phase shift of pulsation in deep cerebral areas is observed.

CONCLUSION

Above all, the data considered in the present chapter fairly clearly endorse the existence of pulsation in the closed cranial cavity. The features of parameters of intracranial pulsation were considered, taking into account hydrodynamic relationships in the closed cranial cavity as illustrated in figure 25. Such an approach to the analysis of the experimental material permitted comprehending the general picture of processes transpiring in the closed cranial cavity during the pulsating influx of blood to the cranium under normal conditions as well as during the action of a number of factors, particularly acceleration.

The important feature of periodic changes in cranial blood pooling and intracranial pressure is the fact that their amplitude and form depend primarily on peculiarities of the compensation of changes in blood pooling in the closed cranial cavity as considered in Chapter 2, and not on their evoked parameters--pulse fluctuations of arterial pressure.

The approach used in this chapter to an analysis of the experimental material cannot, however, explain all the aspects of phenomena observed during the pulsed influx of blood to the cranium. It is entirely possible that the reason for this is the somewhat simplified notions of the hydromechanical qualities of the closed cranial cavity which emerge from an analysis of figure 25. It is /144
also possible that in a number of situations, active pulse changes in the tonus of intracranial vessels begin to influence the pulsation of blood pooling and intracranial pressure which under normal conditions are completely masked by a complex array of hydromechanical processes. This hypothesis is confirmed by the data obtained during the action of high magnitudes of accelerations (up to 40 G). However, as we have already stressed, this problem requires further, more refined analysis.

On the basis of the material considered, an important conclusion in the practical sense can be made: an analysis of the parameters of intracranial pulsation, i.e., pulse fluctuations of intracranial pressure and cranial blood pooling, can yield valuable information on the condition of the intracranial circulatory system. In this respect, the spectral method for evaluating the form of pulse waves is of particular interest. Data on the amplitude and phase of their harmonic components, aside from a quantitative expression of oscillation form, can also be used as original material for studying individual links of the cerebral vascular system using the methods of frequency analysis of physical systems applicable to the theory of automatic regulation and for the analog modeling of these links.

CHAPTER 4. NATURE OF RESPIRATORY WAVES IN THE CLOSED CRANIAL CAVITY UNDER NORMAL CONDITIONS AND UNDER GRAVITATIONAL STRESSES. THIRD-ORDER WAVES

Intracranial electroplethysmography and electromanometers connected to the /145
subarachnoid space are generally used to record periodic fluctuations synchronous with respiratory movements and similar to respiratory changes in the blood volume of other parts of the body that are recorded by means of electroplethysmography and mechanoplethysmography (fig. 69). Consequently, the cerebrovascular system is no exception in this respect.

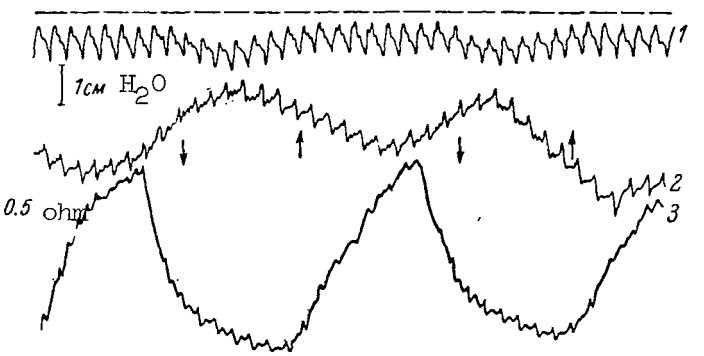

Figure 69. Respiratory waves of intracranial pressure (1), intracranial EPG (2), and respiratory waves of the EPG of the front paw in a dog (3).

Acute experiment. The arrows pointing downward indicate inspiration; those pointing upward, expiration. Time marker - 1 sec

It is common knowledge that respiratory changes in the blood volume of various parts of the body result from several factors, the main ones being the suction exerted by negative pressure in the chest, which promotes the outflow of venous blood during inspiration, and reflex elevation of arterial pressure in a certain phase of the respiratory cycle due to the increased frequency of cardiac contractions and constriction of the arterioles. These factors are also partly responsible for the occurrence of respiratory fluctuations in the cerebral blood volume. However, respiratory waves in the cerebrovascular system have some unusual features as compared with other parts of the body. These are caused by the nature of the hydromechanical relations in the closed cranial cavity.

We shall consider in this chapter the characteristics of respiratory waves in the cerebrovascular system, their role in ensuring normal intracranial circulation, and the dynamics of these waves during gravitational stresses. In addition to the respiratory waves, we shall also examine third-order waves in the cerebrovascular system.

Section 1. Respiratory Waves in the Intracranial Cavity Under Normal Conditions

The existence of respiratory waves in the intracranial cavity was first observed by Magendi. Two years later Ecker (1844) specifically investigated this /146
phenomenon and concluded that during inspiration an increase in pressure in the vertebral veins below the diaphragm increases the blood volume of the vertebral sinuses, thus causing the CSF to flow into the cranial cavity. During expiration the vertebral sinuses are emptied and the fluid returns to the vertebral cavity. Two years later Richet (1846) also concluded that during the respiratory cycle a certain amount of subarachnoid fluid "overflows" from the cranial cavity into the vertebral cavity and then returns.

Subsequent studies (Berthold, 1869; Salathe, 1876; Mosso 1881; Knoll. 1886; Nagel', 1889; Reznikov and Davidenkov, 1911; Becher, 1922; Ewig and Lullies, 1924) produced new but quite contradictory factual material on the origin and nature of respiratory waves in the cranial cavity. For example, Becher writes that "the cerebral circulation is caused by pendulum-like fluctuations of a certain amount of CSF between the cranium and distended spinal sac and by the compensatory outflow of venous blood" (Becher, 1922, p. 325). According to this author, respiratory fluctuations of CSF pressure in the cerebral and spinal cavities spread in wavelike fashion, level out near the foramen magnum; and then spread in waves down to the lumbar region. Thus, the source of the respiratory changes in the cranial blood volume is the fluctuations of pressure in the cerebral venous system.

Ewig and Lullies recorded the respiratory fluctuations of lumbar pressure /147
in human beings with a photomanometer and found that "the respiratory pulse in the cranium" depended in many of the individuals they examined mainly on respiratory fluctuations of pressure in the venous plexuses of the spinal cavity. Thus, according to these authors, contrary to Becher, respiratory fluctuations of pressure in either the cerebral or spinal veins, depending on the type of respiration, may play the leading role in the formation of CSF movements. A third view on the origin of respiratory waves in the cranium was put forward at the same time as the above two views (Mays, 1882; Nagel', 1889; Reznikov and Davidenkov, 1911; others). In this view the respiratory waves of the cranial cavity and intracranial pressure have an arterial origin.

Continued research with the help of better methods (Ryder et al., 1952; Bowsher, 1953, 1960; Moskalenko and Naumenko, 1957; Belekhova, 1958; others) and our own recent studies are very helpful in resolving the above contradictions and they afford a general picture of the phenomena in the cerebrovascular system arising from respiratory movements.

Simultaneous recording of EPGs of the cranial and spinal cavities and intracranial pressure shows that respiratory movements are accompanied by fluctuations of the blood volume in the cranial and spinal cavities in the opposite direction, that the cranial blood supply decreases during inspiration but increases during expiration. Changes in the blood volume and CSF pressure in the cranial cavity during respiration have opposite directions, whereas the directions of the fluctuations of CSF pressure and blood volume of the spinal cavity coincide (fig. 70).

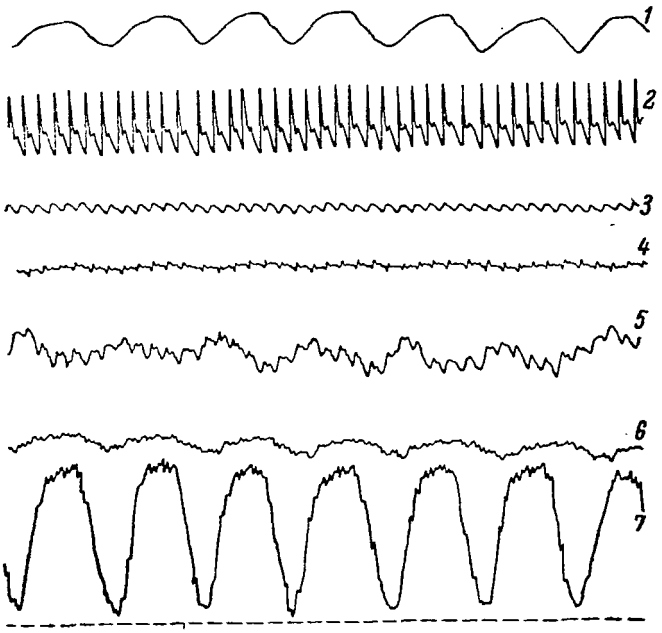

Figure 70. Phase correlations of respiratory waves in the cerebral circulation of a dog.

Acute experiment. 1. respiratory movements of the chest; 2. arterial pressure; 3. blood pressure in arteries at the base of the cranium (measurement by Hürthle's method); 4. intracranial pressure; 5. intracranial EPG; 6. pressure in the lumbar segment of the spinal column; 7. spinal EPG. Time marker - 1 sec.

The amplitude of the respiratory waves of CSF pressure in cats and dogs ranges, according to our data, from 1 to 4 cm H_2O, which is consistent with the findings of O'Connell (1943) and Belekhova (1958). The amplitude of the respiratory changes in the intracranial EPG in the same animals ranges from 0.05 to 0.2 percent of the total resistance between the electrodes (Moskalenko and Naumenko, 1957). The amplitude of the respiratory waves is not the same in different species of animals and in man. Respiratory changes in the cranial blood volume, according to the data that we obtained jointly with P. I. Pesennikova and A. A. Shurubura, occur in the higher reptiles, birds, and mammals (where they are most pronounced). In man, respiratory changes in the cranial blood volume and intracranial pressure are slight under normal conditions, and sometimes they are absent altogether (Becher, 1888; Anders, 1922; Moskalenko et al., 1964c). The shape of the respiratory waves of the cerebral blood volume and intracranial pressure differs considerably from that of the mechanogram of respiratory movements of the chest, whereas the respiratory waves of the spinal blood volume have the same shape (fig. 71).

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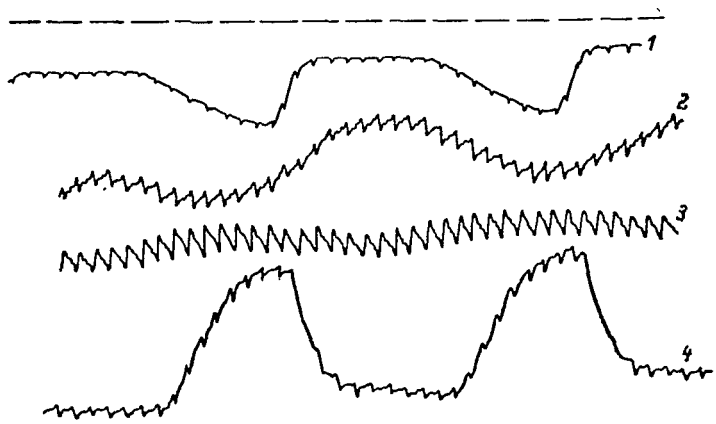

Figure 71. Shape of respiratory waves of the intracranial EPG and intracranial pressure in a rabbit during respiration with sharp inspiration.

Acute experiment. 1. chest mechanogram; 2. intracranial EPG; 3. intracranial pressure; 4. spinal EPG.
Time marker - 1 sec.

These then are the data on the characteristics of the respiratory waves in the cranial cavity. But what do these characteristics determine? As noted above, changes in blood flow due to respiration are typical of both the arterial and venous systems. It is necessary, therefore, to begin by ascertaining in which of these systems change in blood flow is responsible for the origin of respiratory waves of the cerebral blood volume and intracranial pressure. In light of the general ideas on intracranial hemodynamics, it is reasonable to suppose that respiratory changes in pressure in both the arterial and venous systems are theoretically capable of bringing about changes in intracranial /149
pressure, changes in the cerebral blood volume and movement of the CSF between the cerebral and spinal cavities. However, respiratory fluctuations of blood pressure in the arteries at the base of the cranium are usually very slight, like the respiratory waves on the arterial pressure curves in the common carotid artery (fig. 70). On the other hand, the respiratory waves on the intracranial EPG and intracranial pressure curves are much more pronounced. A clear-cut indicator of the magnitude of the respiratory waves may be the ratio of their amplitude to the amplitude of the pulse waves.* Consequently, the possibilty of respiratory changes arising in the intracranial hemodynamics due to the respiratory waves of systemic arterial pressure is quite unlikely under normal conditions.

*

The magnitudes of the amplitudes of the respiratory waves on the curves shown in fig. 70 cannot by themselves be compared owing to the uneven amplification of the different channels of the recording apparatus.

However, one cannot completely rule out the possibility that the arterial system influences the development of respiratory changes in the cerebral blood volume. This influence can be achieved through active changes in the tone of the cerebral arteries synchronously with respiration, the existence of which was demonstrated by Nadareyshvili (1962) who compared the rates of propagation /150
of the pulse wave in the arteries at the base of the cranium in different phases of the respiratory cycle. We too observed in some experiments that after several gravitational stresses respiratory fluctuations of pressure in the arteries at the base of the cranium are intensified and in such cases they are more pronounced than the respiratory waves on the curves showing pressure in the central segment of the carotid artery (fig. 72). We observed such phenomena only against a background of increased excitation of the vasomotor and respiratory centers.

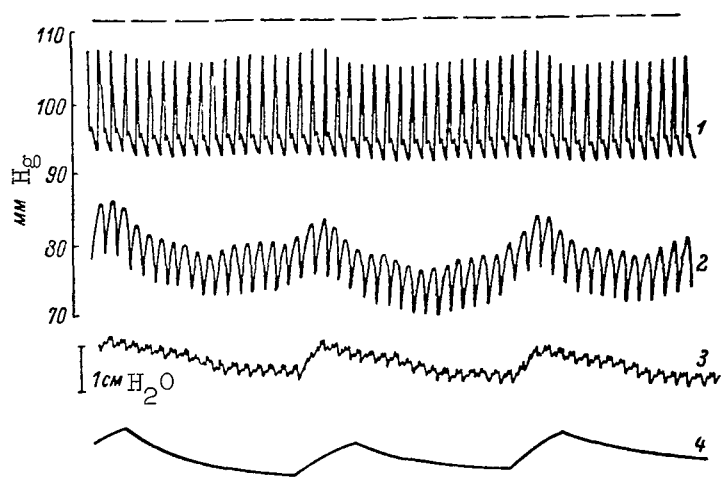

Figure 72. Respiratory waves of general arterial pressure (1), pressure in the arteries at the base of the cranium (2), intracranial pressure (3) and chest mechanogram of a dog after exposure to several longitudinal gravitational stresses of about 1G.
Acute experiment. Time marker - 2 sec.

Let us now examine the possibility of respiratory fluctuations in venous pressure influencing the cerebral blood volume and intracranial pressure. Respiratory changes in blood pressure in the venous system can influence the circulatory parameters of the cranial cavity in two ways. One, they can affect the flow of blood from the cranium because pressure in the superior vena cava rises during inspiration owing to a drop in intrapleural pressure. Two, during inspiration pressure rises in the vertebral venous plexuses located below the diaphragm, which hampers the outflow of blood from the vertebral column. An overflow of blood from the spinal sinuses causes, in turn, some of the CSF to /151
move into the cranial cavity, possibly increasing intracranial pressure in this phase of the respiratory cycle.

To determine which of these phenomena plays the major role, let us examine the other curves shown in figure 70, which are quite typical (about 60 percent of the experiments) of large laboratory animals (dogs, cats, rabbits) in an acute experiment. Comparison of the relative values of the amplitudes of the respiratory waves of intracranial pressure, intracranial EPG, and CSF pressure in the lumbar segment of the spinal column and spinal EPG as well as their phase characteristics reveals that the main factor responsible for the origin of respiratory waves in the cranial cavity is change the blood volume in the vertebral column. It is evident from fig. 70 that the respiratory waves on the EPG curve of the spinal column have the greatest amplitude. Moreover, the coincidence of the phases of respiratory fluctuations of CSF pressure and blood volume of the vertebral cavity, on the one hand, and respiratory fluctuations in CSF pressure in the cranial and vertebral cavities, on the other, as well as the gradual reduction in the amplitudes of the respiratory waves indicate that respiratory changes in the spinal blood volume excite fluctuations of CSF pressure that are transmitted to the cranial cavity. The opposite direction of the respiratory waves of intracranial pressure excited in the spinal cavity promote the outflow of venous blood from the cranium during inspiration. These arguments are also confirmed by the data shown in fig. 71, where the respiratory waves of the spinal EPG completely duplicate the shape of the animal's respiratory movements, whereas the phase of sharp expiration is quite smoothed out on the respiratory waves of the intracranial EPG and intracranial pressure. This suggests that respiratory fluctuations in the cranial blood volume are caused by movement of the CSF between the cerebral and spinal cavities which takes place, as we showed above (page 69, in chapter 2), at limited volume flow rate. If the influence of respiratory movements were exerted solely through the jugular veins, the shape of the respiratory waves of the intracranial EPG would completely duplicate the respiratory movements.

However, the fact that the relative magnitude of the amplitude of the respiratory waves of intracranial waves of intracranial pressure is less than that of the respiratory changes in the cerebral blood volume signifies that the latter changes are somewhat intensified by a drop in pressure in the superior vena cava during inspiration while the respiratory waves of intracranial pressure are weakened. /152

Support for this view comes from other facts as well. During the occlusion of both carotid arteries we never observed any significant change in the magnitude of the respiratory waves in the cranial cavity, but during the occlusion of the superior vena cava or common jugular veins the respiratory waves of the cerebral blood volume mostly decreased (table 8).

This suggests that the leading factor in the formation of the respiratory waves of the cerebral blood volume and intracranial pressure in most (about 60 percent) laboratory animals during an acute experiment is the respiratory changes in blood pressure in the vertebral venous plexuses, but the changes in the cerebral blood volume and intracranial pressure during the respiratory cycle are in the opposite direction. In approximately 30 percent of the animals that we examined, the respiratory waves of the cerebral blood volume and intracranial pressure were in the same direction, signifying that the influence of the respiratory changes in the blood pressure of the cerebral venous system is predominant.

In some animals (about 10 percent), the respiratory changes in the cranial blood volume are not accompanied by similar changes in intracranial pressure. This obviously means that the changes in intracranial pressure arising from the changes /153
in blood pressure in the venous systems of the cranium and spine balance each other.

Examination of the nature of the respiratory changes in the cerebral blood volume reveals that respiratory movements may be one of the mechanisms responsible for maintaining the normalcy of the cerebral circulation. Skokovskiy (1956) was the first to advance this idea. Considerable interest was aroused by the studies of Gamayunov (1927), Khodyakov (1927), Komendatov (1927), and Pavlovskiy (1948), who demonstrated experimentally the significance of respiratory movements in the outflow of venous blood from the cranium. These authors noted the unusual part played by nasal respiration in ensuring normal cerebral blood circulation. The latter indicates that the entire process of respiration beginning with the passage of air through the nose causes respiratory changes in the venous blood flow.

TABLE 8. CHANGES IN AMPLITUDE OF THE RESPIRATORY FLUCTUATIONS OF THE CEREBRAL BLOOD VOLUME AND INTRACRANIAL PRESSURE IN A CAT DURING TEMPORARY OCCLUSION OF THE ARTERIAL AND VENOUS TRUNKS SUPPLYING THE BRAIN WITH BLOOD.

Experimental Conditions	Relative magnitude of the respiratory waves in the cranial cavity (according to the data from 8 experiments)	
	blood volume (percent of normal)	intracranial pressure (percent of normal)
Occlusion of the common carotid arteries	95-100	90-100
Occlusion of the common jugular veins	35-55	60-80
Occlusion of the superior vena cava	15-35	40-50

We rarely observed respiratory waves on the intracranial EPG in human beings under normal conditions, but after 3 or 4 intensified respiratory movements, the level of the cranial blood volume usually dropped while intracranial pressure decreased (fig. 73). These findings are evidence that respiratory movements influence the outflow of blood from the cranium, one of the links in the chain of processes making for normal intracranial blood circulation in man, although under normal conditions this fact is probably of slight importance owing to adapation to the vertical position of the body.

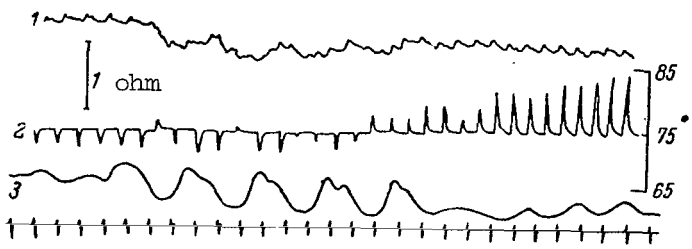

Figure 73. Change in level of the cerebral blood volume (1) and cardiac rate (2) in a man after several deep respiratory movements (3)

Time marker - 1 sec.

It is quite possible that the effect of respiratory movements on the cranial blood volume, as noted by Ewig and Lullies (1924), varies with the type /154 of respiration because the relative effect of respiratory changes in venous pressure in the cranium and vertebral column on the respiratory waves of the cranial blood volume and intracranial pressure is not the same during abdominal and thoracic respiration.

Thus, the foregoing data indicate that the respiratory waves in intracranial circulation may be caused by three factors, the most important being respiratory change in the venous blood volume of the cranial and spinal cavities. Both processes cause changes in the cranial blood volume in the same direction and changes in intracranial pressure in the opposite direction. In some cases, according to our data, excitation of the vasomotor and respiratory centers produces marked changes in the tone of the cerebral arteries synchronous with respiratory movements, which may also influence the respiratory waves of the intracranial EPG and intracranial pressure.

Section 2. Influence of Gravitational Stresses on Respiratory Changes in the Cerebral Blood Volume and Intracranial Pressure

The redistribution of blood due to gravitational forces, as mentioned above, affects mostly the venous system. These forces must therefore be expected to exert a marked influence on the respiratory waves of the intracranial EPG and intracranial pressure.

Judging from the data presented in the foregoing paragraph, it is reasonable to assume that respiratory changes in the cerebral blood volume and intracranial pressure will intensify with the flow of blood to the head and diminish when the blood flows out as a result of gravitational forces because the level of venous pressure and respiratory changes therein are obviously directly related. Our experimental data (Moskalenko et al., 1963, 1964a) are completely consistent with this assumption.

In the case of negative gravitational stresses of the order of 1G, immediately after the beginning of the action the respiratory waves of the intracranial EPG increase three- to fourfold while the respiratory waves of intracranial pressure increase one and one-half- to twofold. In the case of positive stresses, the respiratory waves of the intracranial EPG and intracranial pressure decrease sharply and sometimes even disappear (fig. 61). In the case of longitudinal gravitational stresses ranging from 1 to 6G, the amplitude of the respiratory waves continues to change, but not as much as in the 0.4 to 1G range.

Changes in the amplitude of the respiratory waves of the intracranial EPG and intracranial pressure normally do not coincide with changes in the respiratory waves of the chest mechanogram (fig. 74). Sometimes following several /155
transverse gravitational stresses (10 to 15G) we observed a sharp increase in the amplitude of the respiratory waves of intracranial pressure. This increase was accompanied by a change in amplitude of the respiratory movements in the opposite direction on the chest mechanogram (fig. 75). In all likelihood the absence of a parallelism between the changes in the respiratory waves in the vascular system of the intracranial circulation and the chest mechanogram is due to the fact that the changes in intrapleural and intraperitoneal pressures responsible for the respiratory waves and the scope of the respiratory movements of the chest are not proportional to each other because the pressure changes are caused not only by change in the perimeter of the thoracic cavity but also by movements of the diaphragm.

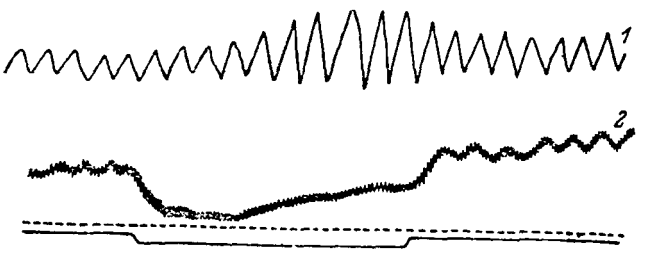

Figure 74. Change in amplitudes of the respiratory waves of a chest mechanogram (1) and intracranial EPG (2) in a cat during longitudinal acceleration of 0.6G.

Acute experiment. 1. intracranial EPG; 2. chest mechanogram. Time marker - 1 sec.

According to the data that we obtained jointly with G. B. Vaynshteyn and I. I. Kas'yan, the respiratory waves of intracranial pressure change considerably in response to lateral accelerations. As the acceleration intensifies, the /156
respiratory waves temporarily cease or decrease sharply due to respiratory standstill, but they reappear as soon as the rotation is steady. Starting with acceleration of 4 to 6G their amplitude, as a rule, increases five- to twenty-fold above the original level. At the same time the respiratory waves on the mechanogram curve decrease sharply as compared with the normal level. The dynamics

of the amplitude of the respiratory waves of intracranial pressure and intracranial EPG in the course of gradually intensifying acceleration is shown in fig. 76. The dynamics of the amplitude of the respiratory fluctuations in intracranial pressure is the same up to acceleration of 4OG (fig. 65). When the action is halted, the respiratory waves become normal within 0.5 to 1.5 minutes. Sometimes this happens suddenly, as shown in fig. 75, apparently because of change in the type of respiration.

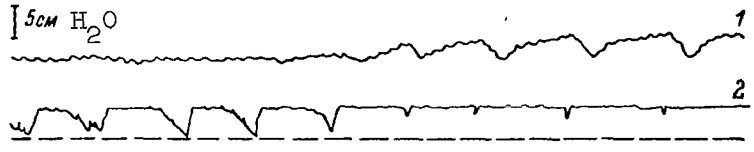

Figure 75. Correlation between the amplitude of the respiratory waves of intracranial pressure and respiratory movements in a dog 20 sec after lateral acceleration of 10 units.

Acute experiment. 1. intracranial pressure; 2. chest mechanogram. Time marker - 2 sec.

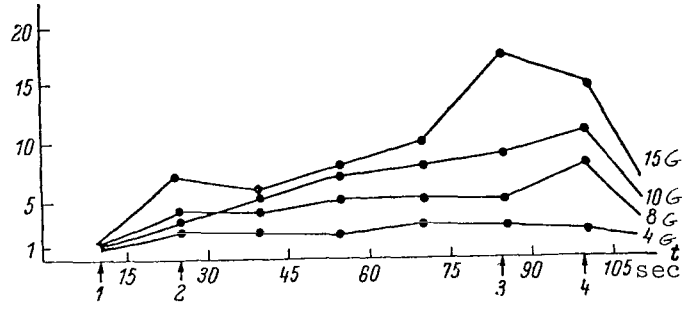

Figure 76. Dynamics of the amplitude of the respiratory waves of intracranial pressure in a dog subjected to lateral accelerations.

Abscissa - time elapsing since the start of the experiment; ordinate - value of the amplitude (in relation to the original). 1. start of centrifuge; 2. steady rotation; 3. start of deceleration; 4. halt.

What is the reason for this substantial increase in the respiratory waves during lateral accelerations? The following is a possible explanation. Substantial lateral accelerations give rise to a spasm of the rima glottidis (Armstrong, 1954; Vokhmyanin, 1963; others). It is quite possible that the /157

respiratory fluctuations of intracranial pressure and intracranial EPG increase as a result of this phenomenon because in this case respiratory movements of narrow scope will cause marked fluctuations of intrathoracic pressure. Consequently, the respiratory fluctuations of venous pressure will likewise increase in both the superior vena cava and inferior vena cava.

To demonstrate the correctness of this assumption, G. B. Vaynshteyn, I. I. Kas'yan, and I ran a special series of experiments to observe the dynamics of the respiratory waves of intrathoracic pressure during lateral accelerations under a variety of conditions. Simultaneous recording of the respiratory waves of intracranial and intrathoracic pressures showed that the amplitudes of the respiratory waves in these systems increased proportionally in response to the accelerations (fig. 77). The respiratory movements of the thoracic cavity meanwhile generally decreased. Following a tracheotomy below the rima glottidis, the increase in the respiratory waves in these systems as the accelerations were intensified to 7 to 9G was much less pronounced than during normal respiration (fig. 77).

These data indicate that spasm of the rima glottidis during lateral accelerations plays an important role in increasing the respiratory fluctuations of intracranial pressure. However, this is not the only cause of increase in the respiratory waves of intracranial pressure because after a tracheotomy there is still some intensification of the respiratory waves of intracranial and intrathoracic pressures during accelerations of more than 7 to 9G. Can this be caused by spasm or compression of the air passages at other levels of the respiratory system? This matter requires further study.

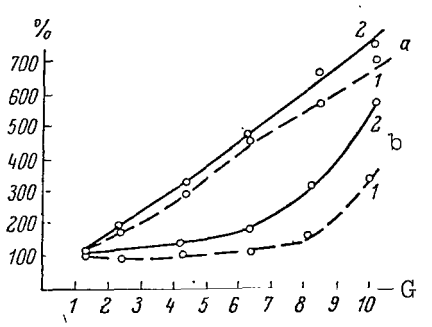

Figure 77. Relationship between the amplitudes of the respiratory waves of intracranial (1) and intrapleural (2) pressures before (a) and after (b) tracheotomy during lateral accelerations.

Abscissa - acceleration (in G); ordinate - amplitude of respiratory waves (as percent of original level)

We may conclude from the foregoing that change in the amplitude of the respiratory waves of the cerebral blood volume and intracranial pressure during /158

longitudinal and lateral accelerations is closely connected with the respiratory fluctuations of intracranial pressure and is therefore passive and mechanical in origin. As acceleration intensifies, so increases the influence of the mechanics of the respiratory act on intracranial blood circulation, despite the fact there are marked disturbances in the respiratory system itself during such actions. The relatively swift and complete restoration of the respiratory waves of the intracranial EPG and intracranial pressure even after sharp lateral accelerations indicates that the latter do not cause a rupture of pulmonary tissue with a pneumothorax.

Section 3. Characteristics of Third-Order Waves in the Cerebrovascular System

It is common knowledge that systemic arterial pressure is characterized not only by pulse and respiratory fluctuations but also by third-order waves called Meyer waves. These waves are thought to be related to the rhythms of the vasomotor center.

Ragozin and Mendel'son (1880) were the first to describe these waves in the intracranial circulation. Some time later Reznikov and Davidenkov (1911) also noted the presence of third-order waves in individuals with cranial defects. They found that the waves were intensified by emotional factors.

We too observed such changes in the cerebral blood supply in acute and chronic experiments on animals (Moskalenko and Naumenko, 1959; Moskalenko et al., 1964b). Third-order waves on an intracranial EPG are regular fluctuations with a period of 0.2 to 0.9 min. Under normal conditions these waves are slight in anesthetized animals (rats, rabbits, cats, and dogs). Their amplitude exceeds respiratory fluctuations in the blood supply one and one-half- to twofold (fig. 78). However, under certain circumstances these waves increase markedly and sometimes exceed the respiratory changes three- to fourfold. We observed this after several longitudinal gravitational stresses of about 1G (fig. 78) and after asphyxia (fig. 39). In the latter case, the fluctuations in the blood volume of the cranial and spinal cavities, which correspond to the third-order waves, move, like the respiratory waves in these cavities, in opposite directions.

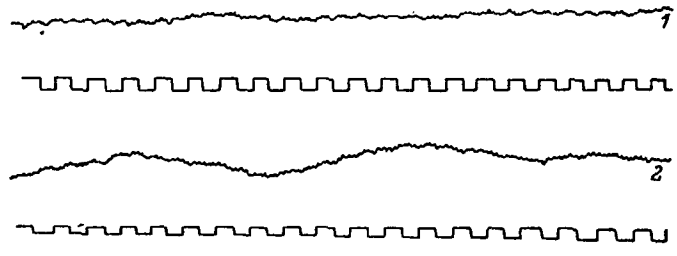

Figure 78. Third-order waves of an intracranial EPG in a rat.

Acute experiment. 1. at the start of the experiment; 2. after exposure to several longitudinal accelerations; Time marker - 1 sec.

We also observed third-order waves in persons with implanted electrodes. During recording of the EPG from subdural electrodes third-order waves as manifested in periodic changes in the level of the intracranial EPG, and the amplitudes and shapes of the pulse waves were pronounced while the patient was sleeping calmly but they disappeared when he was awakened (fig. 79). During recording of the EPG from implanted electrodes, third-order waves were observed both while the patient was awake and while he was sleeping calmly (fig. 79). The third-order waves of the intracranial EPG recorded from implanted electrodes differ in appearance, as is evident in fig. 79, from these waves recorded from subdural electrodes. /159

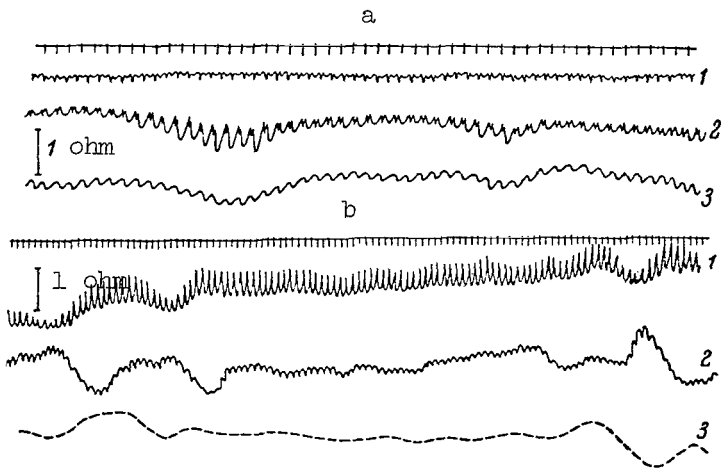

Figure 79. Correlation between third-order waves of the intracranial EPG and dynamics of oxygen tension in a person lying quietly.

a. recording of EPG from subdural electrodes during (1) wakefulness and calm sleep (2); 3. oxygen tension during calm sleep. b. recording of EPG during wakefulness from electrodes implanted in brain tissue (1); 2. oxygen tension in the region lying between the electrodes; 3. result of graphic differentiation of this curve.
Time marker - 1 sec.

The origin of the third-order waves in the cerebrovascular system is still quite obscure. It is not known whether these occurring in the brain correspond to the like changes in systemic arterial pressure. The third-order waves in all likelihood are caused by changes in the tone of the cerebral arteries associated with periodic activity of the vasomotor center. This assumption is supported by facts showing that these waves become intensified by actions that increase the tone of the vasomotor center (figs. 39, 78) and by other facts indicating that the parameters of the pulse waves of the intracranial EPG change in different phases of the third-order waves (fig. 79,a). /160

Of interest in this connection is Copechen's hypothesis (1962) that third-order waves are a reflection of the processes in an automatic circuit that regulates the blood circulation. Myakawa's view (1965) is also interesting. The author analyzes from the standpoint of self-regulation theory Cushing's phenomenon - when CSF pressure rises above the level of blood pressure in the cerebral arteries, periodic fluctuations take place in systemic arterial pressure. Myakawa presented an equivalent diagram of a circuit generating these pressure fluctuations which includes a feedback element. He demonstrated experimentally the validity of this circuit. Myakawa came to what we regard as an important conclusion, namely, that one of the links in the circuit generating fluctuations in systemic arterial pressure is change in oxygen tension in brain tissue. This conclusion is consistent with the results of research demonstrating a connection between the third-order waves and the periodic fluctuations of oxygen tension in brain tissue.

Kovalenko (1961, 1962) showed that oxygen tension in brain tissue recorded by the polarographic method changes periodically more or less with a frequency close to the frequency of the third-order waves in the cerebral vascular system. We recorded such fluctuations of oxygen tension in human beings. However, a direct comparison of the fluctuations of oxygen tension with the intracranial EPG waves corresponding to the third-order waves failed to reveal any coincidence (fig. 79). On the other hand, Cooper (1963) by simultaneously recording the local cerebral blood flow rate (with thermistors) and oxygen tension in brain tissue and, using the methods of electrical differentiation and integration of the resulting curves, showed that the first derivative of the curve reflecting changes in oxygen tension in brain tissue corresponds to the fluctuations of the local cerebral blood flow rate. We found a similar correlation between /161
the third-order blood volume waves in a limited portion of brain tissue and the fluctuations of oxygen tension there. This was the result of graphic differentiation of the oxygen tension curve (fig. 79).

Thus, it would seem that the local third-order waves in the blood vessels of the intracranial cavity are related to the rate of change in oxygen tension in the particular region of the brain. This suggests, in turn, that the periodic changes in intracranial circulation under study are determined by the fluctuations of oxygen tension in brain tissues, with the vascular reaction depending on the rate of change in oxygen tension.

The indicated correlation between the periodic fluctuations of the cranial blood volume and oxygen tension is not significant in as far as the origin of the third-order waves is concerned because this correlation was established only during local recording of changes in blood circulation and oxygen tension in the frontal regions of the brain. A comparison of the curves reflecting changes in the intracranial EPG and oxygen tension recorded from subdural electrodes does not confirm this pattern (fig. 79). In this case the changes in the blood volume of the pial vessels, which correspond to the third-order waves, depend on the magnitude rather than on the rate of change in oxygen tension. Moreover, there is a lack of facts showing a connection between the third-order waves of systemic arterial pressure and similar changes in the intracranial circulation, as discussed above.

Thus, the question of the origin of the third-order waves in the cerebral vascular system must still be considered a moot one. It is possible, however, that information on the relationship between local changes in circulation and oxygen tension will eventually provide the key to its solution. One feasible step is to elucidate the correlation between the general and local changes in the intracranial hemodynamics, which correspond to the third-order waves, on the one hand, and similar changes in systemic arterial pressure, on the other.

CONCLUSION

This chapter examined the characteristics of respiratory waves and third-order waves in the intracranial circulation and their dynamics under gravitational stresses.

Analysis of the respiratory waves of the cerebral blood volume and intracranial pressure shows that the shifting of the CSF between the cranial and spinal cavities plays a major role in the origin of these waves. The data on /162
the third-order waves available to us indicate that the changes in blood volume which correspond to the third-order waves are also compensated by the flow of the CSF between the cranial and spinal cavities.

The materials presented in this chapter show that respiratory movements promote intracranial circulation. The respiratory waves of the cerebral blood volume and intracranial pressure undergo considerable changes during gravitational stresses, reflecting to some extent changes in the cerebral blood supply during the action of this spaceflight factor.

Thus, analysis of the dynamics of respiratory fluctuations of the cerebral blood volume and intracranial pressure during gravitational stresses may provide important information on the state of the intracranial circulation under these conditions.

CHAPTER 5. ACTIVE PROCESSES IN THE CEREBRAL CIRCULATION DURING GRAVITATIONAL STRESSES

Many recent studies on cardiovascular activity during gravitational stresses /163
now provide a more or less complete picture of changes in the blood volume during the action of this spaceflight factor. Some indirect evidence indicates that the cerebral blood flow is extremely vulnerable under these conditions. However, specific studies on the effects of accelerations are few in number. Our knowledge of the subject is still limited to the data which show that the changes in blood circulation that occur during accelerations are marked and that tolerance of the cerebrovascular system for positive and negative gravitational stresses is not the same (Henry et al., 1951; Erbslöh, 1955; Beckman, 1956; Klimovskiy, 1963; Lamb, 1964; Gauer and Neury, 1964). The mechanisms governing the changes and the compensatory possibilities are still obscure.

The purpose of this chapter is to discuss the dynamics of the cerebral blood volume in response to gravitational stresses. This information will later be of help in solving the problem of cerebral blood flow regulation under such influences and in elucidating the underlying physiological mechanisms.

Section 1. General Characteristics Of The Dynamics Of The Cerebral Blood Volume During Gravitational Stresses

Recordings of intracranial EPGs in dogs during rotation on a centrifuge during gradual increase in acceleration (about 0.15 G/sec) showed that with a /164
negative load at the start of rotation the cerebral blood volume differs little from the original level (Moskalenko et al., 1962, 1964a), then changes markedly, after which it remains the same despite further acceleration (figure 80). The values of the accelerations at which the level of the blood volume ceases to change ranges, according to the data from 8 experiments, from 1.2 to 1.8 G.

With increase in positive stresses to 6 to 7 G, the level of the intracranial EPG continues to deviate and the blood volume level does not become stabilized (fig. 80).

A comparison of the dynamics of the level of the intracranial EPG obtained in these experiments with the data set forth in chapter 2, which show that the passive increase in the cerebral blood volume is proportional to the longitudinal gravitational stress, indicates that with negative stresses at the start of rotation there is active compensation aimed at normalizing the blood volume /165
level, but this compensation is impaired by any additional increase in acceleration, and the blood fills the cranial cavity to its maximum capacity as determined by its mechanical properties.

After positive acceleration the outflow of blood from the cerebral venous system intensifies, and the blood flow continues until blood pressure in the arteries at the base of the brain exceeds that in the veins. A decrease in the blood volume during positive gravitational stresses seems to produce a decrease in the tone of the cerebral vessels and the subsequent reduction in the blood volume slows, starting with accelerations of a certain intensity, as

can be seen in figure 80. Thus, the magnitude of the maximum positive accelerations during which the intracranial circulation continues is much higher than that of the negative accelerations. For example, according to the data of Henry et al., 1951, during positive accelerations of about 5 to 6 G arterial pressure drops to zero, but perfusion pressure persists because pressure in jugular veins drops to -60 mm Hg. Beckman (1956) observed that the cerebral blood flow persists during marked positive accelerations. Klimovskiy (1963) in chronic experiments on cats showed that the rate of blood flow in the veins proceeding from the cranium decreases slightly when acceleration is increased to 7 G.

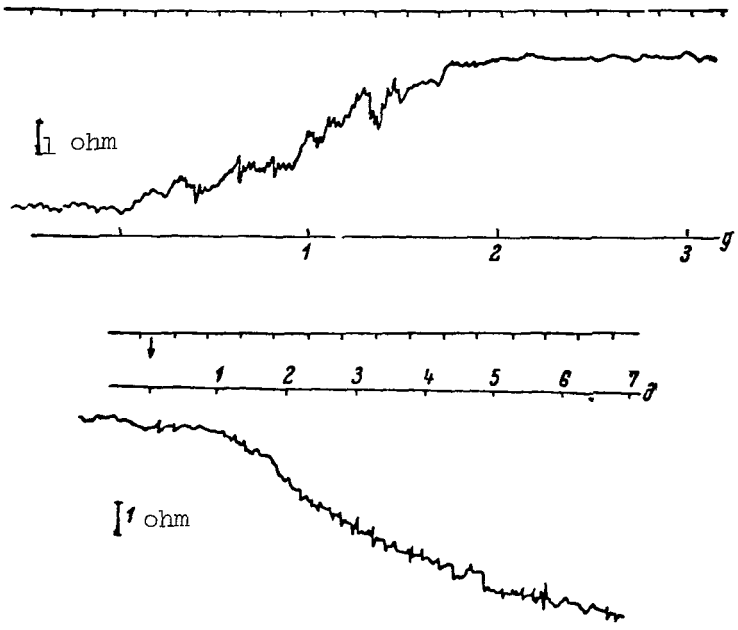

Figure 80. Change in level of an intracranial EPG in a dog during gradual increase in negative (top) and positive (bottom) longitudinal accelerations.

Chronic experiment. Time marker - 1 sec.

All this demonstrates that the effect of longitudinal accelerations on the cerebral circulation is largely dependent on their direction in relation to the blood flow in the extraorgan arteries that supply the brain with blood. When the directions of the acceleration and arterial blood flow coincide, the cranial cavity of dogs overflows with blood during comparatively mild acceleration (-1.2 to 1.8 units). A sharp deterioration in the cerebral blood supply is to be expected after this. The forces of acceleration and arterial pressure when moving in different directions are mutually compensatory so that the brain continues to be supplied with blood until accelerations of 5 to 7 G. Both

negative and positive accelerations produce active cerebrovascular reactions aimed at normalizing changes in the blood volume.

During lateral accelerations in a back-chest direction or vice versa, the cerebral blood volume usually increases as G. B. Vaynshteyn, O. G. Gazenko, I. I. Kas'yan, A. A. Shurubura, and I have shown. However, the dynamics of the level of the cerebral blood supply and intracranial pressure in the period of acceleration and deceleration of the centrifuge is not the same when the animal /166 is positioned differently in relation to the direction of rotation or when the rotation becomes stabilized at different rates.

If the animal's head is in the direction of rotation of the centrifuge, a rapid start (about 1.2 G/sec) results first in some decrease in intracranial pressure, then in a rapid increase followed a little later by stabilization. However, if the start is slow (about 0.6 G/sec), intracranial pressure scarely changes, after which it increases and stabilizes a few seconds after steady rotation conditions is achieved (fig. 81). The level of the intracranial EPG changes in the same way.

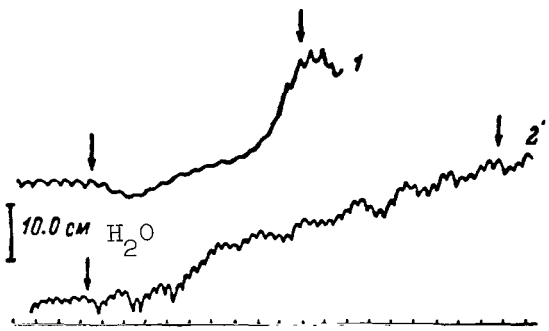

Figure 81. Change in intracranial pressure in a dog during rapid (1) and slow (2) increase in acceleration to 10 G. Acute experiment. The arrows designate the start of rotation and achievement of steady conditions.

Time marker - 1 sec.

When the animal's head is facing in a direction opposite to that of the rotation, regardless of whether the centrifuge is accelerated rapidly or slowly, the levels of the blood volume and intracranial pressure begin to rise immediately after the start and achieve maximum values by the time steady rotation conditions are achieved.

The relationship between the dynamics of the levels of the cerebral blood supply, intracranial pressure, rate of acceleration of the centrifuge, and orientation of the animal in relation to the direction of rotation can be explained as follows. When the centrifuge is started, two gravitational stresses act on the animal - increasing lateral and brief longitudinal accelerations. When the animal's pelvis faces the rotation, the longitudinal component helps to increase the cerebral blood volume and intracranial pressure, but it prevents this when the animal's head faces forward in the direction of the rotation of the centrifuge. These phenomena are more pronounced when the centrifuge is acce- /167 lerated quickly because the longitudinal component of the action is greater.

However, regardless of the speed with which the centrifuge is accelerated or the orientation of the animal, both the cerebral blood volume and the intracranial pressure grow because of the intensifying lateral component of the acceleration. At the same time, as noted by several authors (Armstrong, 1954; Vokhmyanin, 1963; others), there is usually breath holding in the inspiration phase and an increase in tracheal, pleural, and intraabdominal pressures. Meanwhile there is a pooling of blood in the lungs, abdominal organs, and, possibly in the cranial cavity. The increased intrathoracic and intraabdominal pressures are apparently transmitted to the venae cavae, and because the pressure in the jugular veins is slight, as pointed out above (p. 103 in chapter 3) even a small increase in pressure hampers the outflow of venous blood which causes, in turn, venous hyperemia of the brain and spine and elevation of intracranial pressure (Bedford, 1935; Ryder et al., 1952; others).

This is illustrated by figure 82, which shows the resemblance between the dynamics of intrapleural, tracheal, and intracranial pressures in an animal both with intact respiration and with respiration through a tracheal tube. In the latter case the intensity of the rise in intrapleural and intracranial pressures decreases. The dynamics of the EPG, as can be seen in figure 82, differs somewhat from the other processes recorded. With due allowance for the fact that acceleration of the centrifuge in this series of experiments was slow, it is fair to conclude that here too, as in the case of lateral accelerations, active cerebrovascular reactions serve to compensate the changes in level of the cerebral blood volume. /168

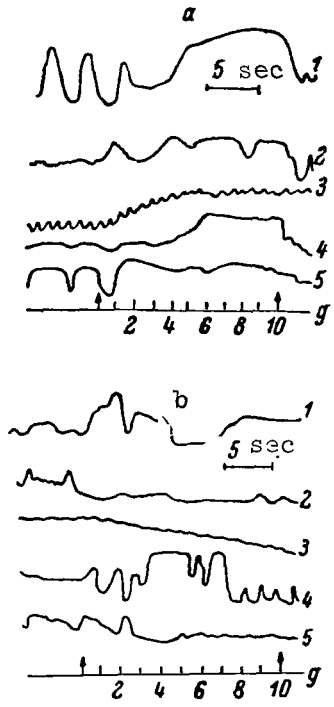

Figure 82. Change in intracranial EPG (1), intracranial (2), intrapleural (3), intratracheal (4) pressures and chest mechanogram (5) in a dog after acceleration of the centrifuge.

Acute experiment. a. before tracheotomy; b. after tracheotomy. The arrows designate the start of rotation and achievement of steady conditions.

After lateral accelerations of the same intensity, the levels of the cerebral blood volume and intracranial pressure change comparatively little. During slight accelerations of 8 to 15 G, the maximum values of both indices are reached 20 to 30 seconds after achievement of steady rotation conditions; during substantial accelerations, immediately after they are achieved. Intracranial pressure drops slightly before the start of deceleration.

Maximum values of the cerebral blood volume and intracranial pressure depend both on the magnitude of the lateral acceleration and on the direction (chest-back or back-chest). With low accelerations the rise in intracranial pressure is slight. The rise is greatest after accelerations ranging from 6 to 12 G, but on reaching a certain limit (after accelerations of about 15 to 20 G), intracranial pressures ceases to rise (fig. 83). It is evident from the figure that this phenomenon sets in sooner after acceleration in a back-chest direction. The cerebral blood volume also increases to a certain point and thereafter changes little even if the acceleration is intensified. It is interesting to note that the degree of increase in cerebral blood volume after the acceleration reaches a steady value depends on the position of the animal in relation to the direction of rotation of the centrifuge, i.e., on the direction of the longitudinal component of the acceleration at the time the centrifuge is started.

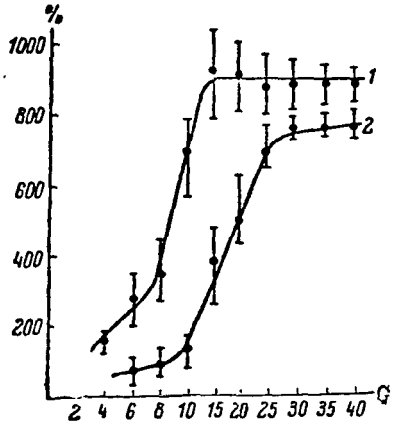

Figure 83. Relationship between the maximum change in the level of intracranial pressure in a dog and the intensity of lateral acceleration.

Acute experiment. Abscissa - intensity of acceleration (in G). Ordinate - intensity of intracranial pressure (in percent of normal). The vertical lines designate 95 percent confidence limits of the mean of 8 measurements. 1. back-chest acceleration. 2. chest-back acceleration.

The dynamics of the cerebral blood volume and intracranial pressure during lateral accelerations of unchanged magnitude can be related in part to the characteristics of respiration and blood flow in the pulmonary circulation in response to lateral accelerations (Watson et al., 1960; Kiselev, 1962; Marotta et al., 1962; Wood et al., 1963). Simply stated, during accelerations of low and medium intensities (up to 10 to 15 G) the blood is driven by centrifugal force from the pulmonary artery into the vessels of the lungs which then go into spasm. Pressure increases in the venae cavae and right auricle, apparently resulting in a rise in intracranial pressure. During intense accelerations the hydrostatic pressure of the blood overcomes the resistance caused by spasm of the pulmonary vessels. Along with despositing blood in the viscera this empties the venae cavae. At the same time the stroke volume of the left ventricle decreases sharply. Consequently, the levels of the cerebral blood volume and intracranial pressure become stabilized despite increasing lateral acceleration.

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These processes also help to account for the difference in the dynamics of intracranial pressure between acceleration in different directions (chest-back or back-chest), as shown in figure 83.

While the dynamics of the levels of the intracranial EPG and intracranial pressure upon acceleration of the centrifuge is similar in the different experiments, the dynamics of these indices when the centrifuge is decelerating varies considerably from animal to animal even when the rate is about the same. In some animals there is a sharp drop in cranial pressure immediately after the start of deceleration, whereas in others it rises slightly at first and then drops, although it remains high when the centrifuge comes to a full stop. We noted similar characteristics on the intracranial EPG curves.

It is evident that while the centrifuge is decelerating the same forces are acting on the animals as when it is accelerating, i.e., decreasing lateral and incipient longitudinal accelerations. The latter changes direction from that which prevails during the acceleration. It is noteworthy that these forces act against a background of hypoxia and changes in the systemic and intracranial blood circulation and after marked shifts in the balance of the biologically active substances (Khazen and Vaysfel'd, 1962; Gyurdzhian et al., 1963; others) that result from the effects of lateral acceleration.

All this together with the different reactions of the animals to acceleration apparently determines the dynamics of the indices recorded while the centrifuge is decelerating. Our data show that the dynamics of the cerebral blood volume is significantly affected at this time by the direction of the accompanying longitudinal component of the accelerations. For example, with the animal's head oriented in the direction of rotation, the negative longitudinal acceleration /170
arising during the deceleration prevents the level of the blood volume from returning to normal and it remains high for some time after the centrifuge comes to a stop. On the other hand, with the animal's head oriented opposite the direction of rotation, the longitudinal component of the accelerations promotes the outflow of blood from the cranium and in the same animal the level of the blood volume falls below the original even before the centrifuge stops, after which it rises quickly (fig. 84).

The levels of the EPG and intracranial pressure usually return to normal 1 to 3 min after the action of low and medium accelerations and 3 to 7 min after the action of intense ones.

Some fluctuations of intracranial pressure often occur around the original level after the centrifuge stops. The duration and nature of the restorative period of the processes recorded seem to depend on the active restorative reactions of the cerebral blood vessels.

The above data were obtained, as already mentioned, in acute experiments on dogs under moderately deep anesthesia, but we also observed similar relationships in experiments on other animals - rabbits and rats. The only difference /171
is that active compensation was less pronounced in these animals and in the dogs. A special series of experiments on dogs with electrodes implanted in the skull yielded results similar to those obtained in an acute experiment, but the

increase in the cerebral blood volume of the nonanesthetized animals was not as large as in the anesthetized animals.

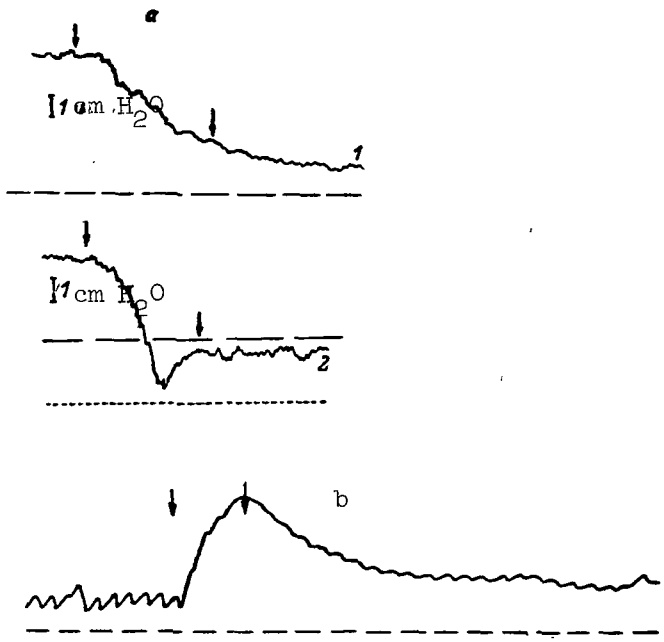

Figure 84. Change in level of the cerebral blood volume during deceleration of the centrifuge. a- acute experiment on a dog whose head is facing forward (1) and backward (2) in relation to the direction of rotation of the centrifuge. The broken line designates the level of the cerebral blood volume before the action. b- during observation on a human being (the electrodes to record an intracranial EPG were placed on the skin). The arrows designate the start and end of the deceleration of the centrifuge.

Time marker - 1 sec.

Our observations on human beings exposed to 8 to 10 G of lateral accelerations showed that the level of the intracranial EPG recorded by applying electrodes to the head also changed considerably. However, the changes differed from those noted in the experiments on animals. As the acceleration increased, the human cerebral blood volume slightly decreased, but rose above the original level (fig. 66) when the centrifuge decelerated. The magnitude of the rise and fall varied from subject to subject.

The nature of the dynamics of the human cerebral blood volume is very probably related to the effect of the longitudinal component of the accelerations because the position of the subject in the centrifuge is not strictly perpendicular to the direction of the acceleration and during rotation the positive longitudinal component appears and apparently causes the blood volume to decrease. It may be that the longitudinal acceleration that arises during the acceleration and deceleration of the centrifuge also plays a part in the process. If the subjects are placed with their feet in the direction of rotation, longitudinal acceleration may cause more blood to flow from the head when the centrifuge is accelerated and to flow back when it is decelerated. Evidence for this assumption comes from the data obtained during abrupt slowing down of the centrifuge which show that the cerebral blood volume increases significantly at this time (fig. 84).

In summing up our findings on the dynamics of the cerebral blood volume and intracranial pressure during lateral gravitational stresses, we should like to point out that under experimental conditions involving a centrifuge the dynamics of these indices is determined by two sets of factors. First, against a background of an increased cerebral blood volume and intracranial pressure resulting from lateral acceleration, the accompanying longitudinal component alters the levels of the values recorded during the speeding up and slowing down of the centrifuge and when the conditions are steady provided that the body is at an angle to its direction. The direction of this longitudinal acceleration is particularly significant.

The longitudinal component causes blood to flow out of the cranium in the /172
acceleration phase and this partly compensates the changes in the cerebral circulation produced by the lateral acceleration, and vice versa. In the deceleration phase the longitudinal component either helps to restore the original levels of the recorded indices or it delays the restoration. It will be noted that the relatively rapid restoration of the original level of the intracranial EPG and intracranial pressure after intense accelerations is another indication of the high resistance of the intracranial blood circulation to mechanical factors, although structural changes in the walls of the cerebral vessels apparently persist after intense accelerations, as demonstrated by Prives (1963) for other vascular regions.

Second, active reactions of the cerebrovascular system obviously arise as a result of change in the cerebral blood volume and intracranial pressure and as a result of interoceptive reflexes and development of cerebral hypoxia due to deterioration in the blood supply and decreased oxygenation of the blood. Of importance too are the reactions elicited by longitudinal acceleration during the speeding up and slowing down of the centrifuge. These reactions determine the original level of cerebrovascular tone during lateral acceleration under steady rotation conditions.

Thus, the combination of the processes of active regulation and those caused by mechanical forces makes the degree of impairment of the cerebral circulation during lateral accelerations dependent both on the magnitude of the stress applied during the steady rotation conditions and on the acceleration of the centrifuge. The rate of restoration of the original indices varies with

the deceleration conditions of the centrifuge. It is thus fair to assume that the degree of impairment of the cerebral blood volume may be reduced by choosing the optimum combination of longitudinal and lateral accelerations. This can be done by appropriate orientation of the body to the direction of the acceleration.

The data examined in this section on the dynamics of the level of the cerebral blood volume during longitudinal and lateral accelerations indicate that a passive mechanical factor plays an important part in altering the blood supply at this time. Besides passive change in the level of the cerebral blood volume, there are also active changes. But it is quite difficult, in our opinion, to say anything concrete regarding the origin of these changes, especially the /173
underlying active reactions of the cerebral vessels. This is due, first, to the fact that gravitational stresses generally provoke a series of active reactions by several systems, including the cardiovascular and cerebrovascular. It is extremely difficult to single out the reaction of the cerebrovascular system. Second, experiments with a centrifuge have shown that the nature of the passive change is complex. This hampers the task of differentiating the passive and active changes in the cerebral blood volume and intracranial pressure.

Thus, the data obtained during marked longitudinal and lateral accelerations throw light only on the general characteristics of the changes in the cerebrovascular system.

We shall now examine in some detail the nature of the dynamics of the cerebral blood volume and intracranial pressure in a range of low longitudinal accelerations as part of a comprehensive study of the active reactions of the cerebrovascular system. Analysis of the material will help to identify the mechanical component of the reaction and to evaluate the specificity of the observed active reactions for the portion of the vascular system under investigation.

Section 2. Characteristics Of The Active Reactions Of The Cerebrovascular System To Low Longitudinal Accelerations

We studied in acute and chronic experiments on animals and during observations on man the characteristics of active compensation of change in the cerebral blood volume during longitudinal accelerations of ±1 G. To identify the active changes in the level of this blood volume, we created gravitational stresses by rapidly changing the position of the animal's body on a revolving table. Passive changes, as shown in chapter 2, took place exponentially and against this background it was easy to distinguish the active changes.

Figure 85 shows the changes in level of the intracranial EPG in a cat during increasing accelerations. It is evident that several seconds after an intensity of 0.4 to 0.5 G was achieved the exponential nature of the changes became impaired and the level tended to return to what it was before the action. The fact that the dynamics of the level of the intracranial EPG was at variance /174
with the theoretical calculations testified to the existence of active processes in the cerebrovascular system. Simlar active changes in the level of the intracranial EPG varied in prominence among the different species of animals and human beings (figs. 86, 87, 88).

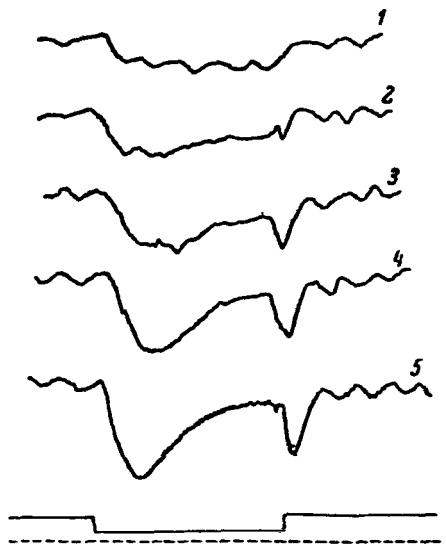

Figure 85. Change in level of an intracranial EPG in a cat during positive accelerations.
Acute experiment. 1- 0.2G; 2- 0.4 G; 3- 0.6 G; 4- 0.8 G; 5- 1 G.
Time marker - 1 sec.

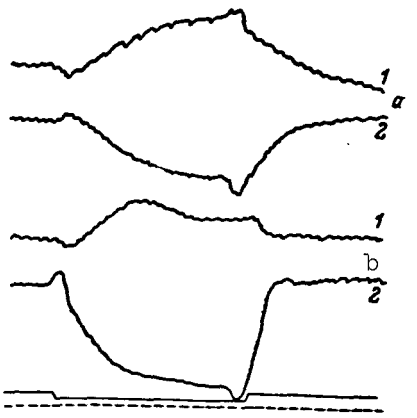

Figure 86. Change in level of an intracranial EPG in a frog (a) and lizard (b) during negative (1) and positive (2) accelerations of 1 G.
Time marker - 1 sec.

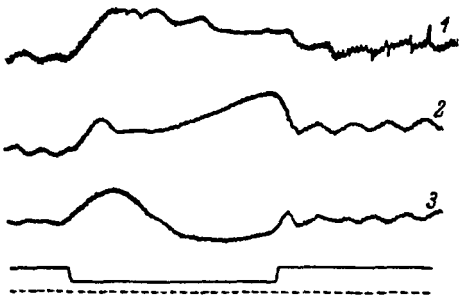

Figure 87. Change in level of an intracranial EPG in several species of animals during negative accelerations of 0.6 G.
Acute experiment. 1- pigeon; 2- rabbit; 3- cat.
Time Marker - 1 sec.

We failed to observe active normalization of level of the cerebral blood volume in lower vertebrates - frogs and turtles (fig. 86). Partial, far from complete compensation occurred in lizards and pigeons (fig. 86 and 87). In mammals, 5 to 10 sec after the start of the action the level was almost completely normal. In cats and dogs, the normalized level persisted 30 to 40 sec during the acceleration and sometimes as much as 60 sec, whereas in rabbits and rats it persisted only 10 to 20 sec. When /175 the acceleration was increased, the duration of the phase of active normalization became shorter. Compensation of the level of the cerebral blood volume was longest and most complete in human beings (fig. 88). With both positive and negative accelerations, continuation of the action resulted in a rise in the level after the normalization phase. This rise was generally accompanied by a sharp increase in the amplitude of the pulse and respiratory waves.

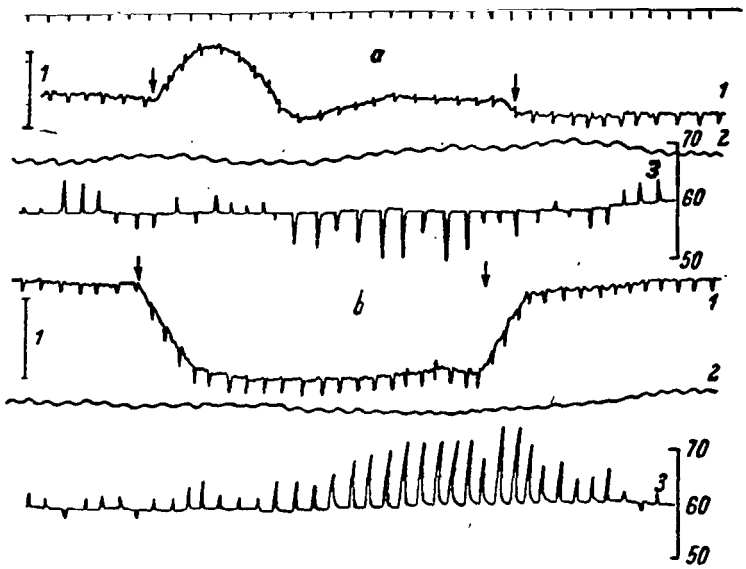

Figure 88. Change in level of an intracranial EPG (1), oxygen tension (2), and cardiac rate (3) in a human being during negative (a) and positive (b) accelerations of 0.5 G. The EPG was recorded from subdural electrodes.

The arrows designate the start and end of the action.
Time marker - 1 sec.

The above-described active changes in level of the intracranial EPG were more pronounced after negative accelerations, especially in human beings (fig. 88).

In some experiments with mammals, especially cats, when positive accelerations achieved certain intensities (about 0.8 to 1 G), the level of the intracranial EPG changed in the opposite direction. During accelerations of about 0.2 to 0.3 G, changes in the direction of the level of the intracranial EPG were as expected, indicating that the cerebral blood volume decreased (Moskalenko et al., 1964a). With stresses of about 0.8 to 1 G the passive change was completely masked by the active processes, which not only normalize the blood volume level but also give rise to hypercompensation. /176

The cerebral blood volume often decreases sharply for a few seconds after negative accelerations. This phenonemon, like transient spasm of the cerebral vessels, occurred in our experiments on frogs, turtles, lizards, chickens (fig. 86) and in daeply anesthetized mammals when active normalization of the level of the blood volume was insignificant or absent (fig. 89).

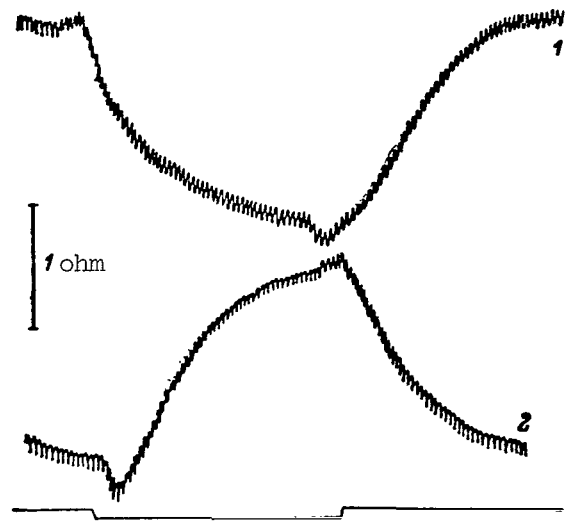

Figure 89. Change in level of an intracranial EPG in a deeply anesthetized cat during positive (1) and negative (2) accelerations of 1 G.
Time marker - 1 sec.

In the case of positive accelerations, a similar transient change in the cerebral blood volume occurred, as a rule, immediately after the action ceased. This was also observed in experiments on turtles, lizards, chickens, and sometimes cats and dogs, regardless of the depth of anesthesia (fig. 90), and during observations on human beings (91), but in the latter, only when the EPG was recorded from implanted electrodes.

Figure 90. Change in level of an intracranial EPG and intracranial pressure in a cat at the moment when positive acceleration was halted. /177

1. intracranial pressure; 2. EPG; 3. rate of change in intracranial pressure $\left(\frac{dP_1}{dt}\right)$.
Time marker - 1 sec.

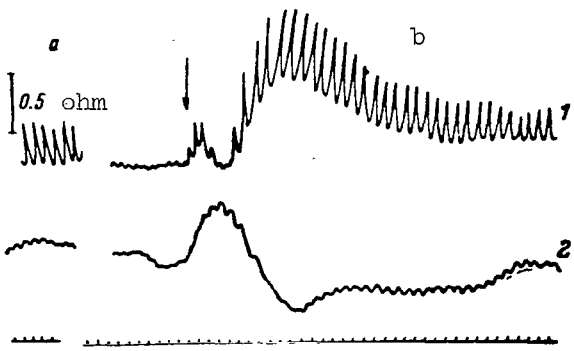

Figure 91. Change in level of an intracranial EPG (1) and oxygen tension (2) in a human being after the cessation of positive acceleration. The EPG and polarograms were recorded from electrodes implanted in brain tissue.

a. before the action; b. during restoration of the original position of the body. The arrows designate the time the action was halted.

Time marker - 1 sec.

In a series of experiments on cats and dogs, the dynamics of intracranial pressure and pressure in the cervical and lumbar segments of the spine was recorded simultaneously with the intracranial EPG. The experiments showed that changes in intracranial pressure and pressure in the cervical and lumbar segments of the spine are proportional to the intensity of the acceleration and that they occur immediately after the action is started (table 9). /178

TABLE 9. MAXIMUM VALUES OF THE CHANGE IN PRESSURE IN DIFFERENT PARTS OF THE CEREBROSPINAL CAVITY DURING POSITIVE ACCELERATIONS LASTING 1 MINUTE (BASED ON 10 MEASUREMENTS)

Intensity of acceleration (in G)	Magnitude of change in pressure (in cm H_2O)		
	within the cranium	in the cervical segment of the spine	in the lumbar segment of the spine
0.2	0.5-1.5	-	0.8-2.0
0.6	2.0-3.0	0.1-0.5	2.0-4.0
1.0	3.0-5.0	0.3-1.0	4.0-7.0

Changes in the levels of intracranial and lumbar pressures, as shown in figure 92, are related and in the opposite direction, but pressure in the cervical segment of the spine changed only insignificantly.

The dynamics of CSF pressure in the cranial and vertebral cavities during acceleration, as shown in figure 92, was much less pronounced than the changes in level of the intracranial EPG. The lack of a parallelism between the changes in CSF pressure and cerebral blood volume, as noted in chapter 2, is further evidence of active changes in the level of this blood volume during longitudinal accelerations such as living organisms encounter under natural conditions.

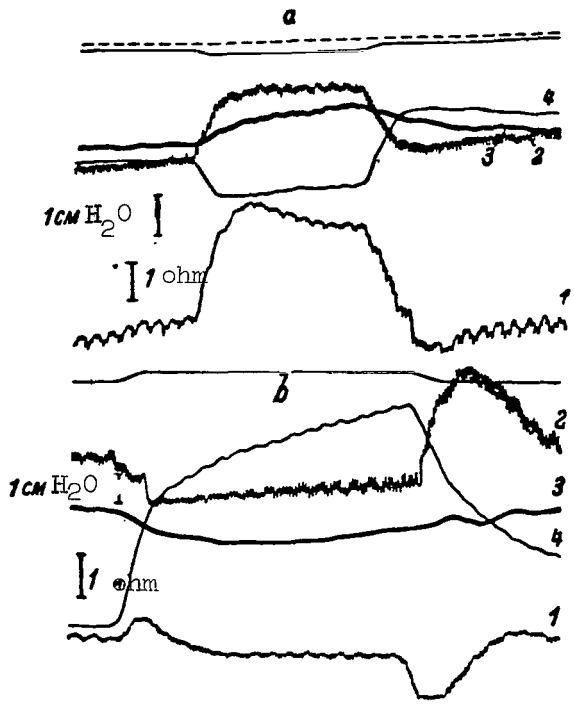

Figure 92. Changes in the levels of the intracranial EPG (1), intracranial pressure (2), pressures in the cervical (3) and lumbar (4) segments of the spine in a cat during negative (a) and positive (b) accelerations of 0.6 G.

Acute experiment. Time marker - 1 sec.

It is fair to conclude from the facts set forth above that in most of the species of animals investigated low accelerations give rise to active changes in the cerebral blood volume. These changes are very likely the result of adaptation to the gravitational stresses occurring in nature. The reactions can be divided into two groups: (1) active normalization of the blood volume level occurring some time after the start of the action and most pronounced during negative accelerations; (2) temporary changes in the level of the blood volume level occurring at the beginning or end of the action in relation to the direction of the action. /179

Active reactions of the first type occur in the higher animals and man, while those of the second type are most characteristic of the lower vertebrates in which they arise, as a rule, both at the beginning and at the end of the action regardless of its direction. Although we sometimes observed active reactions of the second type in the higher species of animals and in man, they generally did not occur unless the action was in a given direction. The deeply anesthetized animals constituted an exception.

The data that we obtained in investigations on representatives of various /180
classes of animals and on human beings show that the minimum values of the negative accelerations at which there are active changes in the level of the intracranial EPG range from 0.3 to 0.6 G. The upper limit at which there is active compensation of the cerebral blood volume supply varies considerably from species to species. In amphibians, reptiles, birds, and some mammals (rats and rabbits), we were able to achieve these limits using a revolving table. But in experiments on cats and dogs these limits exceeded 1 G and then only in the experiments involving a centrifuge. A comparison of the averaged data obtained in the experiments on several representatives of four classes of vertebrates (fig. 93) indicate that there is a relationship between the tolerance of negative accelerations and the level of development of the central nervous system as well as the mode of life of the animals. To construct the graph shown in figure 93, data on the upper limit of the acceleration at which compensation of the cerebral blood volume in man is still possible were taken from the studies of Howard /181
and Glaister (1964), who investigated the cerebral blood flow using radioactive krypton, and of Wood et al. (1963), who investigated the threshold of visual impairment during longitudinal accelerations.

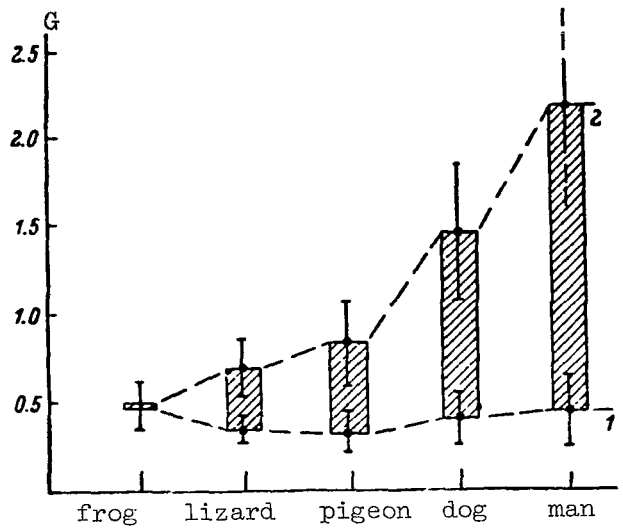

Figure 93. Regions in which active changes in the cranial cavity blood supply were manifested in various vertebrates and human beings during negative accelerations.

1. lower limit; 2. upper limit. The vertical lines show 95 percent confidence limits of mean values of the lower and upper limits. Ordinate - intensity of acceleration.

On the basis of our data we assume that the limits of active compensation of the level of the cerebral blood volume during longitudinal accelerations vary not only with the level of CNS development but with the ecological characteristics and functional state of the organism. This is proved by the results of experiments that we performed jointly with Z. I. Barbashova, I. I. Kas'yan, A. A. Shurubura on three groups of rats. The first group was kept in an ordinary cage. The second group was kept for several weeks in special chambers that restricted the vertical mobility. The third group was acclimatized to hypoxia. A comparison of the data obtained for the animals exposed to negative accelerations showed that the threshold of inclusion and the upper limit of active compensation of the level of the intracranial EPG differed considerably (table 10).

TABLE 10. THRESHOLDS OF INCLUSION AND MAXIMUM VALUES OF NEGATIVE ACCELERATIONS AT WHICH ACTIVE CHANGES WERE PERCEPTIBLE IN THE CEREBRAL BLOOD VOLUME OF RATS KEPT UNDER DIFFERENT CONDITIONS.

Animals	Number of animals investigated	Threshold of inclusion of active reaction of the cerebral vessels	Maximum accelerations at which active changes were perceptible in the cerebral blood volume
control	22	0.4-0.6	0.8-1.0
kept under hypoxic conditions	24	0.8-1.0	>1.0
kept under conditions of limited mobility	19	0.3-0.4	0.6-0.8

We noted a similar correlation between the thresholds of inclusions and upper limits of the accelerations at which active compensation occurred in the blood volume when we compared the data obtained from the same groups of animals during positive accelerations. But here the threshold of inclusion of the active reactions was higher than during negative accelerations.

During the acclimatization of rats to hypoxia, as shown by Shurubura et al. (1965), there are significant periodic fluctuations of the cerebral blood volume both under normal conditions and during longitudinal accelerations. This article /182 offered only one of several possible explanations for the effect of acclimatization to hypoxia on active reactions of the cerebral vessels to longitudinal accelerations.

The results of comparing animals kept under conditions of limited mobility with the control are in agreement with the observations of Graveline and McCally (1962) and Miller et al. (1964). These authors found that after prolonged immersion in water or after prolonged immobility human beings are much less able

to tolerate orthostatic tests and they frequently exhibit symptoms of cerebral ischemia.

Thus, the functional state of the organism would seem to exert a significant influence on the active cerebrovascular reactions to longitudinal accelerations. This suggests that prolonged weightlessness can also affect the reactivity of the cerebrovascular system.

The experimental material presented in this section indicates quite clearly that there are two kinds of active changes that arise in the cerebral blood volume as a result of the redistribution of blood caused by brief longitudinal accelerations. These active changes may be a manifestation of the activity of the mechanisms formed in the course of the evolutionary adapation of living beings to the earth's gravity.

Having demonstrated the presence of active changes in the cranial cavity blood supply and elucidated some of their characteristics, let us now turn to their specificity for the cerebrovascular system.

Section 3. Origin Of Active Changes In The Cerebral Blood Volume During Low Longitudinal Accelerations

It follows from our general ideas on the effects of longitudinal accelerations that there are two kinds of active changes in the cerebral blood volume. First, they may arise from change in the perfusion pressure of the blood, the result of change in the systemic circulation due to gravitational stress. Thus, changes in the cerebral blood volume may be caused by factors external to the cerebrovascular system. Secondly, they may be caused by regional reactions of the cerebral vessels which are specific only for that part of the vascular system. They arise as a result of change in the intracranial circulation during acceleration. /183

Which of these kinds of reactions is responsible for active compensation of the cerebral blood volume during acceleration? The available data suggest that it is caused by autonomous reactions of the cerebrovascular system. The results of simultaneous recording of arterial pressure in the femoral artery and intracranial EPG in cats and dogs (Moskalenko et al., 1964b) show that during longitudinal accelerations of up to 1 G, when there is active compensation of the cerebral blood volume, arterial pressure changes insignificantly and only at the start of the action and after it is halted. This fact is consistent with the data cited above (p.115) on the steadiness of systemic arterial pressure during slight longitudinal accelerations.

It is common knowledge, however, that during slight longitudinal accelerations significant changes sometimes occur in the cardiac rate, apparently the result of reflexes from the baroreceptors in the orifices of the venae cavae. Moreover, we observed tachycardia and bradycardia in persons subjected to positive and negative accelerations, respectively (Moskalenko et al., 1964c). Yet simultaneous recording of an intracranial EPG and of the dynamics of the cardiac rate in man shows that the changes in these indices during gravitational stresses are not related. For example, in the case of negative acceleration of about

0.6 G, bradycardia sets in several seconds after the start of active compensation of the cerebral blood volume, whereas in the case of positive acceleration of the same intensity, the level of the intracranial EPG scarcely changes during the action, despite the development of tachycardia (fig. 88).

All this testifies to the autonomy of active compensation during longitudinal accelerations. For final proof we traced the dynamics of the blood volume in other parts of the body during longitudinal accelerations (Moskalenko et al., 1963). Recording of an EPG of the antebrachium in animals (rats and cats) with /18
the anterior extremity placed at the level of the head showed that during positive and negative accelerations (about 1 G) the blood volume of this part of the body changes only at the start and end of the action, but the level remains steady in the intervening interval (fig. 94). We obtained similar results when recording a chest EPG during the same actions (fig. 94).

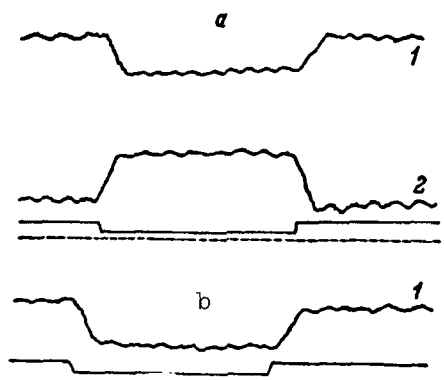

Figure 94. Change in level of a chest EPG (a) and EPG of the forepaw (b) in a rat exposed to positive (1) and negative (2) accelerations of 1.0 G.

Acute experiment. Time marker - 1 sec.

Thus, the factual material more or less confirms our conclusion as to the autonomy of the active reactions of the cerebrovascular system during slight longitudinal accelerations. Nevertheless, more information is needed on the localization of these reactions because the regulatory processes in the cerebral vessels are known to function independently of one another in different parts of the vascular system. For example, according to Mchedlishvili et al. (Mchedlishvili and Ormotsadze, 1962; Mchedlishvili et al., 1962), at least three areas can now be distinguished in the cerebrovascular system which differ from one another with respect to regulation: (1) extraorgan arteries (internal carotid and vertebral) which transport the blood to the brain, (2) arteries of the pia mater, and (3) blood vessels in brain tissue. The next task, therefore, is to determine at which level of the cerebrovascular system the above reactions of the cerebral vessels take place.

As adequate solution of the problem is now difficult to achieve for technical reasons. It would require the study, in isolation, of the characteristics of the reactions of different vascular regions and even of individual blood vessels. And in doing so it would be necessary to take into account the functional characteristics of the brain structures which these vessels supply with blood. We shall therefore limit ourselves below only to considering the relative participation of the three main divisions of the cerebrovascular system distinguished by Moskalenko et al. in realization of active changes in the cerebral blood volume. /185

Of considerable interest in this connection is a comparison of the data on the dynamics of the cerebral blood volume during negative accelerations with the data on the nature of the reaction of the pial arteries during temporary occlusion of the superior vena cava, as observed by Mchedlishvili et al. (1962) with the help of serial microphotography. This phenomenon is partly similar to the effect of negative accelerations because in both instances the main factor influencing the cerebral vessels is interference with the outflow of venous blood from the cranium.

Mchedlishvili et al. found that the pial vessels constrict immediately after the superior vena cava is occluded but dilate about 1 minute later. This indicates that active compensation of the change in the cerebral blood volume, which takes place several seconds after the start of acceleration, may be caused by the reactions of the pial arteries. Support for the assumption that the pial arteries play a major role in this respect during gravitational stresses comes from the data that we obtained by simultaneously recording an intracranial EPG and blood pressure in the central and peripheral portions of the internal carotid artery (the dynamics of the difference between these pressures provides information on changes in the tone of the arteries at the base of the cranium).

It is evident from figure 95 that the difference in pressures in the central and peripheral portions of the internal carotid artery does not change significantly during negative accelerations, i.e., the tone of the arteries at the base of the cranium is virtually unchanged. An intracranial EPG recorded at the same time reveals the active reactions of the cerebrovascular system.

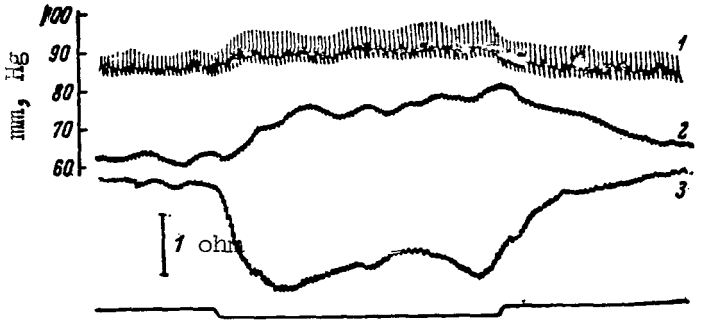

Figure 95. Correlation between pressures in the carotid artery (1) and in the arteries at the base of the cranium (2) and intracranial EPG (3) in a dog exposed to longitudinal accelerations of 0.8 G.

Pressure in the arteries at the base of the cranium was recorded by Hürthle's method. Time marker - 1 sec.

A comparison of the data that we obtained by recording changes in the cerebral blood volume in man from subdural and implanted electrodes likewise suggests that the pial arteries are much more involved in the active changes occurring in the level of the intracranial EPG than are the arteries in the deep-lying divisions of the brain. Whereas changes in the level of the EPG recorded from subdural electrodes dring brief gravitational stresses clearly reflect the active compensation of changes in the cerebral blood volume, the intracranial EPG recorded from implanted electrodes undergoes changes only at the start and end of the action, remaining unaffected during the intervening interval. /186

Thus, the factual material at our disposal shows that the pial arteries play a leading role in effecting active changes in the cerebral blood volume during brief longitudinal accelerations. This is not an unexpected conclusion because the pial arteries are in direct contact with the CSF and therefore active change in the lumens is quite possible. Moreover, since pressure drops sharply in the pial arteries of small and medium diameter (Symon et al., 1963), change in their tone is a very effective regulator of the intensity of the cerebral flow.

While acknowledging the importance of the role played by reactions of the pial arteries in bringing about active changes in the cerebral blood volume, it would nevertheless be wrong to think that this is the only site of the active processes that arise in the cerebral vascular system during gravitational stresses. It is quite probable that under certain conditions the arteries at the base of the cranium and the vessels of the deep-lying portions of the brain also participate in the active reactions. Nor can the possiblity of active involvement of the venous portions of the cerebrovascular system be ruled out.

New types of active reactions of the cerebral vessels set in especially when the action is lengthened. For example, during prolonged negative accelerations of from 0.6 to 1.0 G we observed that following the phase of compensation of changes in the cerebral blood volume indicative of constriction of the cerebral vessels, the blood volume increased rapidly 0.5 to 1 min after the start of the action (Moskalenko et al., 1964a), just as happened in the experiments of Mchedlishvili et al. (1962). This shows that there is a new phase in the active reactions of the cerebral blood vessels which seem to embrace not only the pial vessels but also other parts of the cerebrovascular system. /187

Section 4. Possible Physiological Mechanisms Responsible For Active Changes In The Cerebral Blood Volume During Gravitational Stresses

The physiological mechanisms controlling the cerebrovascular reactions under various conditions are quite difficult to discuss for two reasons. One is that the existing methods are too limited to reveal in full all the characteristics of the reactions to a given stress. The other reason is that the mechanisms that regulate the cerebral circulation are still not sufficiently understood. Consequently, the discussion must be confined to more or less plausible working hypotheses. We shall examine, therefore, only the two best

known phenomena: (1) active normalization of the level of the cerebral blood volume during brief gravitational stresses, and (2) active changes in the level of the cerebral blood volume that arise at the start and end of longitudinal accelerations.

What are the physiological mechanisms that may be responsible for these phenomena? In the light of current ideas on the mechanisms regulating the intracranial circulation, it is reasonable to suppose that active normalization of the cerebral blood volume during longitudinal accelerations is either the result of brain tissue hypoxia caused by interference with the cerebral blood flow or the result of stimulation of the baroreceptors, i.e., it is reflex in origin. Another possiblity is that both mechanisms are involved simultaneously.

Judging by the available facts, it is most unlikely that active compensation of changes is brought about by phenomena associated with impairment of the cerebral blood supply. For one thing, simultaneous recording of oxygen tension in /188
brain tissue and an intracranial EPG in animals and human beings has shown that the first index remains unchanged during the development of active compensation of changes in the blood volume (fig. 88). During longitudinal accelerations of 2 G lasting 1 minute, according to Banchero et al. (1965), oxygen tension in arterial blood also changes little. Moreover, the short latent period (3 to 10 sec) of the reaction of active compensation of changes in the cerebral blood volume indicates that it can hardly be caused by processes associated with impairment of the oxygen supply of brain tissue because hypoxia usually develops over much longer periods of time. We never observed in human beings any disagreeable sensations resulting from active compensation of the cerebral blood volume. Electroencephalograms taken at this time were within normal limits (Moskalenko et al., 1964b).

The foregoing leads one to believe that active normalization of the cerebral blood volume during slight longitudinal accelerations is controlled by reflexes elicited by changes in blood pressure in the cerebral veins and in intracranial pressure because these systems are characterized by the greatest relative changes in pressure. This assumption is supported by numerous morphological studies testifying to the existence of both baroreceptor zones in the venous sinuses and dura mater (Perlin, 1955; Yegorova, 1958; Mikhaylov, 1965; others) and efferent innervation of the pial arteries (Backay, 1941; Legait, 1947; Konstantinovskiy, 1960; others). Mchedlishvili and Ormotsadze (1962) obtained direct experimental data on the existence of reflex constriction of regional cerebral arteries in response to stimulation of the baroreceptor zones in the venous sinuses.

The most likely possibility, therefore, is that a neurogenic mechanism is responsible for active compensation of changes in the cerebral blood volume during gravitational stresses. The duration of the latent period of the compensatory reactions (3 to 10 sec) parallels the duration of the latent period of rapid cerebrovascular reactions of neurogenic nature (Ludwig and Schneider, 1954).

It may be that the reflex circuit which starts with the baroreceptors of the venus sinuses and dura mater and ends in the pial arteries also includes the subcortical formations of the brain because active compensation of changes

in the cerebral blood volume is absent during deep anesthesia, as noted (p. 149). Blinova and Marshak (1963) likewise point out that the neuroreflex activity of the cerebral vessels decreases during deep anesthesia. /189

A comparison of the data that we obtained in experiments on representatives of four classes of vertebrates suggests that neurogenic reactions aimed at compensating changes in the level of the cerebral blood volume during longitudinal gravitational stresses first appear in the higher reptiles.

Analysis of the intracranial hemodynamics reveals that active reactions of the pial arteries in gravitational stresses serve to normalize the hydrodynamic resistance of the cerebrovascular system. As pointed out in chapter 2, the total hydrodynamic resistance of the cerebral vessels depends on the correlation between the volumes occupied by the arterial and venous systems in the cranial cavity. This resistance increases with change in the volume of blood in one of the systems. Active change in the volume of the other system in a direction opposite to that of the first may normalize the hydrodynamic resistance of the cerebral vessels. Thus, it is fair to assume that during longitudinal accelerations active normalization of the level of the cerebral blood volume, as manifested in change in the volume of the pial arteries in a direction opposite to the passive change in the venous blood volume, leads to compensation of the increase in hydrodynamic resistance of the cerebral vessels and is one of the manifestations of the self-regulatory system of the cerebral blood supply.

It seems, then, that active normalization of the cerebral blood volume due to increased venous pressure in the cerebral vessels achieves the same result as in the case of mechanical automatic stabilization of the cerebral blood flow during changes in arterial pressure, as discussed in chapter 2. The only difference is that passive automatic stabilization is brought about by mechanical action of the system with the greater internal pressure (cerebral arteries) on the system with the lower internal pressure (cerebral veins), and vice versa in the case of active normalization, i.e., by action of the system with the lower internal pressure on the system with the greater internal pressure. The latter is possible owing to the mechanism of regulation examined above.

In all likelihood these compensatory reactions do not fully normalize the cerebral blood supply in all cases because it has been found that in dogs, for example, the intensity of the cerebral blood flow with the animal's body in a vertical position and head up may drop as much as 50 percent (Mayerson, 1940). In each of the species of animals that we investigated, active changes in the level of the cerebral blood volume has its own characteristics with respect to both compensation and its duration. /190

The second kind of active reactions observed during longitudinal accelerations consists of transient changes in the blood volume at the start and end of the action. The nature of these reactions suggests that they are based on change in vascular tone in response to change in intravascular pressure which, say many investigators (Fog, 1938; Forbes et al., 1937 ; Folkow, 1956; Thuraw and Kramer, 1959; others) is a property of the smooth musculature, especially of the walls of the cerebral vessels. These reactions occur only when the stresses change, i.e., during sharp passive change in the cerebral blood volume under the influence of

gravitational forces. The shape of the curve reflecting active change in the blood volume that takes place at this time coincides with the curve reflecting change in the rate of acceleration or, more accurately, in the rate of change in the cerebral blood volume and intracranial pressure (fig. 90).

In most cases, active reactions of the second kind in man and animals are very brief, no more than 2 to 4 sec in duration, but these reactions sometimes increase rapidly and persist as long as 15 to 20 sec. Since they cause the vessels to constrict, their increased duration may induce hypoxia because even with transient reactions of this kind there is a decrease in oxygen tension in brain tissue (fig. 91). Therefore, we cannot rule out the possibility that such prolonged reactions give rise to transient ischemic anoxia during longitudinal accelerations, as observed by Rossanigo and Meimery (1961) and Duvoisin et al. (1962). This phenomenon seems to occur quite often. For example, according to Dermiksian (1960), transient syncope caused by ischemic anoxia of the brain occurs during orthostatic tests in 13 percent of the cases. It is noteworthy that in mammals under deep anesthesia, when there is no active compensation of the cerebral blood volume, active reactions of this kind, as shown above, persist and they can be observed both when intravascular pressure increases and when it decreases. This fact supports the assumption that the reactions are a local response of the cerebral vessels to changes in intravascular pressure during gravitational stresses.

A comparison of the data that we obtained in experiments on representatives /191
of four classes of vertebrates suggests that the kind of active cerebrovascular reactions under study is a phylogenetically older type of regulation of the cerebral circulation during gravitational stresses. With increase in the level of organization, the significance of this type of regulation decreases while that of the neuroreflex mechanism characteristic of the higher vertebrates and man grows. However, this assumption requires proof.

The direction of the active reactions of the cerebral vessels, at the start and end of longitudinal accelerations, relative to the passive change in the cerebral blood volume shows that they prevent the cerebral blood volume from changing drastically. Overfilling of the vessels with blood, a potential danger to the vascular walls, is the most serious effect of gravitational stresses.

It is interesting to note in this connection that in amphibians, reptiles, and birds the vascular reactions under study occur both when the cerebral blood volume is increasing and when it is decreasing, whereas in mammals and man the reactions arise only when the blood volume is increasing either at the start or end of the action, depending on the direction of the gravitational stress. Presumably, reactions of this kind are more differentiated in mammals than in other classes of vertebrates.

It is worth noting that these reactions are related to the rate of change in intravascular pressure. Such a relationship between the stimulus and the cerebrovascular reaction is by no means exceptional. As we demonstrated in chapter 4, local changes in the blood supply of the deep-lying portions of the brain bear the same relationship to the rate of change in oxygen tension in brain tissue. The regulatory principle, which is based on the dependency of the effect not on the intensity of the acting force but on the rate of change therein, most likely has important biological significance. This relationship

between the force and the active response may well help to prevent disturbances in the system during extreme stresses because one of the indices of the force of the action is its rate of growth.

We observed still another kind of active reactions of the cerebral vessels during prolonged accelerations - a phase of increasing blood volume of the cranium /19
followed by a phase of active compensation. This phase is probably caused by dilatation of the cerebral vessels resulting from the development of hypoxia because the intensity of the cerebral blood flow, as mentioned above (p. 160), continues to decrease even during slight (about 1 G) negative accelerations, despite active compensation of the level of the cerebral blood volume. A sharp increase in the amplitude of the pulse waves of the intracranial EPG is another indication of dilatation of the cerebral vessels.

Thus, this kind of active reactions of the cerebral vessels can be regarded as reactions of humoral nature. They have been thoroughly studied in recent years (Lassen, 1959; Kety, 1960; Meyer and Gotoh, 1961; others) and are considered by some investigators to be the only kind of active reactions in the part of the cerebrovascular system. With the latter, however, we find it hard to agree in the light of the data presented in this section of our monograph.

CONCLUSION

The data presented in this chapter indicate that the cerebrovascular system is sensitive under normal conditions to gravitational influences and has special mechanisms that ensure compensation of the changes in the intracranial hemodynamics caused by gravitational forces.

Longitudinal and lateral accelerations produce significant changes in the cerebral blood volume and intracranial pressure. These provoke active reactions of the cerebral vessels aimed at compensating these changes. During accelerations below certain intensities they prevent impairment of the cerebral blood supply.

Active reactions of the cerebral vessels are elicited by low longitudinal accelerations of about 0.3 to 0.5 G, such as living things encounter under normal conditions. They also arise during lateral accelerations created artificially and they are one of the factors that affect living organisms during spaceflight.

In this chapter we examined in detail only one group of specific active reactions of the cerebral vessels. These are the reactions that arise in response to slight longitudinal gravitational stresses. They are of three kinds: (1) transient constriction of the cerebral vessels at the start of positive accelerations and end of negative accelerations; (2) active reactions of the cerebral vessels aimed at compensating changes in the cerebral blood supply whose latent period ranges from 3 to 8 seconds; (3) dilatation of the cerebral vessels 20 to 60 seconds after the start of the action.

The threshold of inclusion of the first two kinds of reactions ranges from /193
0.3 to 0.6 G; that of the third, from 0.6 to 1.0 G.

An intensification of longitudinal or lateral accelerations stimulates new active reactions of both the cerebral vessels and other divisions of the cardiovascular system. Possible indications of the inclusion of these reactions are changes in the level of the cerebral blood volume examined in this chapter and changes in the parameters of the periodic fluctuations of these values, pulse and respiratory waves, as demonstrated in chapters 3 and 4.

It is possible that the active reactions of the cerebral vessels, the result of stimulation of the vestibular apparatus, play some role in these processes. The existence of such reactions was shown in the works of Borishpol'skiy (1896), Klosovskiy (1942, 1951), Naumenko and Olesov (1958), and others. Reflexes from various interoreceptor zones seem to be another important factor in regulating the cerebral blood flow during accelerations (Shul'zhenko, 1965). It is also necessary to bear in mind the changes that take place in the systemic and pulmonary circulations, changes in oxygenization of the blood and concentration of various metabolites therein.

It is quite evident, therefore, that the processes observed in the cerebrovascular system during gravitational stresses are quite extensive and that the underlying physiological mechanisms are complex. In this chapter we examined only a few of what we believe to be the most important phenomena involved.

SOME RESULTS

The structure of the cerebrovascular system is responsible for the existence /194
of a complex set of hydrodynamic processes underlying the intracranial circulation. The cerebral blood flow, therefore, is influenced by gravitational stresses, including those encountered by living organisms under natural conditions and during spaceflight.

In studying the problem, one must obviously start with the underlying hydrodynamic processes. The patterns of both the passive and the active changes in the cerebrovascular system caused by gravitational stresses have to be determined. However, our knowledge here is quite limited and based largely on the results of studies carried out many years ago and containing contradictory facts. Thus, the nature of the passive changes in the cerebral circulation and the possibility of active changes during gravitational stresses is still a moot question.

Accordingly, the author of this monograph set out to demonstrate the patterns of change in one of the principal indices of the intracranial circulation, one that is most subjected to gravitational stresses - the cerebral blood supply.

The materials considered show that the volumes of arterial and venous blood and cerebrospinal fluid in the closed cranial cavity experience continuous interrelated changes resulting from cardiac activity, respiration, third-order waves, and such factors as gravitational stress. These changes are governed by two compensatory mechanisms: (1) redistribution of the volumes of arterial and venous blood, and (2) change in the correlation of the total cerebral blood supply and /195
CSF volume present in the submeningeal spaces of the brain. These two mechanisms have different time and amplitude characteristics and they ensure the compensation of both rapid and slow changes in the cerebral blood volume. They also play an important part in maintaining the essential level of the cerebral blood supply by promoting utilization of the pulse wave energy of arterial pressure and respiratory movements for the outflow of venous blood from the cranium. These mechanisms are likewise responsible for mechanical automatic stabilization of the cerebral blood flow. On the basis of the special relationships existing between the volumes and pressures of arterial and venous blood and CSF in the cranial cavity, it was possible to work out the general pattern of the physical correlations in the cerebral circulation, incorporate it in a mathematical model, and program it for a computer.

From the materials presented in chapter 2 it can be concluded that two kinds of changes in the cerebral blood volume are to be expected during gravitational stresses: (1) change in the total cerebral blood volume due to the redistribution of blood, and (2) change in the parameters of the periodic (pulse and respiratory) fluctuations of the blood volume. The most important changes in the intracranial circulation occur during longitudinal accelerations. During lateral accelerations the basic changes are caused by the longitudinal components and by changes in the systemic and pulmonary circulations (chapter 5).

Data on active processes in the cerebrovascular system indicate that two kinds of active reactions can be distinguished during slight and brief accelerations lying close to the threshold of the biological action of this factor.

Reactions of the first kind have a latent period of several seconds and are aimed at normalizing the total cerebral blood volume, while reactions of the second kind occur when the stress is changed, their purpose being to prevent drastic change in the cerebral blood volume. The first set of reactions is presumably characteristic mostly of the higher vertebrates and man, while the other reactions are generally found in the lower vertebrates. However, other active processes appear when the duration and intensity of longitudinal accelerations is increased and during lateral accelerations. These are indicated both by change in the levels of the cerebral blood volume and intracranial pressure and by the dynamics of their periodic fluctuations - pulse and respiratory waves. The parameters of these /196
fluctuations, their amplitude and shape, as shown in chapters 3 and 4, carry information on both the active and passive processes in the intracranial circulation.

Cerebral hypoxia plays an important part in the origin of these reactions, as shown by the onset of a third phase of active change in the cerebral blood volume following an increase in duration of the action.

On the basis of the materials set forth in this monograph and a comparison of them with the data in the literature, we thought it possible to present a flow pattern of the regulation of the cerebral circulation during gravitational stresses as a unique, partly isolated system. Although any representation of a complex set of biological processes in a flow pattern will inevitably, of course, lead to a simplification of the true picture of the phenomena, we tried to avoid distortion in the effort to provide a deeper understanding of the phenomena that take place in the intracranial circulation.

At the present stage in our knowledge of the regulation of the cerebral circulation, it is convenient to look upon our simplified and generalized scheme as a terminal automatic device (fig. 96). Assuming that the blood oxygen level is constant, arterial and venous pressures (chapter 2) can be taken as inputs. The output, of course, is the correlation between the concentration of oxygen and other metabolites in brain tissue and its requirement therefor. These indices obviously depend on the capillary blood flow and, consequently, on the intensity of the cerebral blood supply. The purpose of regulation during various actions on the body, therefore, is to maintain the intensity of the cerebral blood flow at the necessary level when the parameters of the inputs are changed.

Judging by the dynamics of the cerebral blood flow examined in chapter 2, the blood flow in the cerebral capillaries following a change in the parameters of the inputs of the system is kept at a constant level mainly by mechanical automatic stabilization of the flow. In the diagram shown in figure 96, element M performs the stabilization function. The possibilities of such mechanical automatic stabilization are limited. However, the brain is fairly well supplied with nutrients even after rather substantial changes in the parameters of the inputs. The latter is possible thanks to the existence of active regulation of the cerebral blood flow which alters the hydrodynamic resistance of various portions of the vascular bed to changes in the input signals, thereby maintaining the necessary level of the capillary blood flow. In the suggested flow pattern this /197
function is performed by regulators which ensure the compensation of changes in the parameters of the inputs. As noted above, in the present stage of knowledge about regulation of the cerebral circulation at least three independent groups of

regulators can be identified: regional or extraorgan arteries R_1, pial arteries R_2, and deep-lying cerebral arteries R_3. It is quite possible that the cerebral veins are also involved in active regulation of the blood flow. Our flow pattern includes, therefore, a corresponding element R_4.

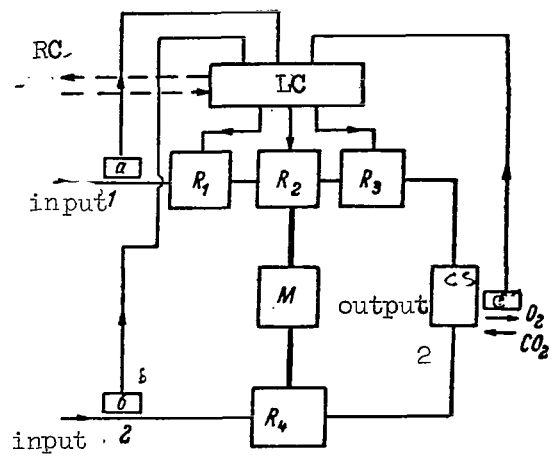

Figure 96. Flow pattern showing the regulation of the cerebral blood supply during gravitational stresses.

R_1, R_2, R_3, and R_4 - regulators of the hydrodynamic resistance of the cerebral vessels; cs - capillary division of the cerebrovascular system; M - unit for mechanical automatic stabilization of the cerebral blood flow; a, b, c - receptor zones controlling the state of the inputs and output of the system; RC - center (or centers) regulating the cerebral circulation; LC - center linking the regulation of the cerebral circulation to other units regulating the cardiovascular system.

All these regulators are controlled by the corresponding center or centers which determine their activity. It is still difficult to say anything definite about the functioning and localization of this center or centers. We should merely like to point out that it (or they) must obtain information about the inputs and output of the system. The state of input 1 seems to be controlled by the carotid zone receptors and by the receptor zones in the region of the bifurcations of the cerebral arteries. These receptor zones control both arterial /198 pressure and the blood chemistry. Presumably the first parameter is the source of information for controlling the tone of the cerebral arteries; the second, for controlling the number of functioning capillaries. The state of input 2 is controlled by the baroreceptor zones of the venous sinus and by the

baroreceptors of the dura mater because the pressure on the dura mater is similar to the pressure experienced by the walls of the veins. The state of the output of the system seems to be controlled by brain structures sensitive to the concentration of metabolites in brain tissue, specifically CO_2 and O_2. These groups of receptors are designated a, b, and c in our diagram.

We mentioned only the principal receptor zones which we believe play a major role in maintaining the cerebral blood flow during gravitational stresses. However, we cannot rule out the possibility of active cerebrovascular reactions elicited by other receptor zones localized in the cerebrovascular system or in other vascular basins.

Information from the receptor zones is transmitted through nerve channels to the regulatory center of centers, whence the control signal enters the executive system - the regulators. The signal also seems to be transmitted to the central control organs of the circulatory system or to the centers they control, thus promoting the compensation of changes in the input parameters from without. The connection between the center regulating the cerebral circulation and the other regulatory units of the cardiovascular system is designated RC.

The diagram shown in figure 96 clarifies some of the processes responsible for maintaining the homeostasis of the cerebral circulation during gravitational stresses. For example, during a drop in arterial pressure or elevation of venous pressure in the vessels transporting blood into or out of the brain as a result of direct or indirect gravitational stress, the intensity of the cerebral blood flow does not change, as would happen in a simple mechanical system (fig. 97, broken lines), but is kept constant within fairly broad limits of change in the input parameters. This constancy is ensured by several mechanisms, the principal ones being the following (fig. 96):

1) Mechanical automatic stabilization of the cerebral blood flow (chapter 2). It keeps the cerebral blood flow constant upon change in the parameters of input 1 to some provisional level I (fig. 97).

2) Active cerebrovascular reactions of neurogenic nature (first and second kinds of reactions, examined in chapter 5). These reactions keep the output steady upon change in the parameters of input 2 and possibly input 1 to level II. /199

3) Active cerebrovascular reactions of humoral nature arising from change in concentration of CO_2, O_2, and other metabolites in brain tissues following some primary decrease in the cerebral blood supply. These reactions maintain the cerebral blood flow upon change in the input parameters to level III.

It is only when changes in the parameters of the inputs exceed level III that the cerebral blood flow decreases and noncompensated hypoxia develops with all the aftereffects.

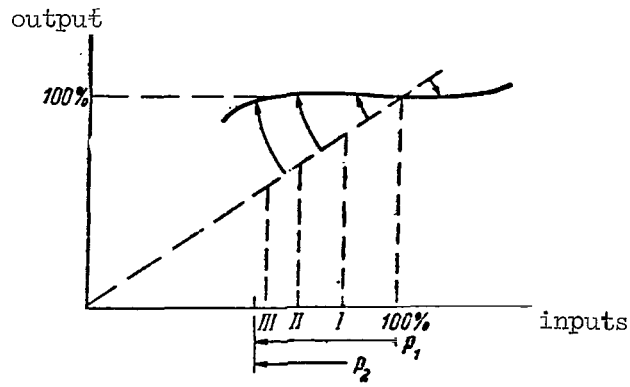

Figure 97. Graph illustrating the working of the flow pattern shown in figure 96.

Absicssa - level of inputs of the system; ordinate - level of the output. The broken lines show the relationship characteristic of a nonregulated system. I, II, and III - levels to which the mechanisms regulating the cerebral circulation are effective.

Thus, the diagram showing the regulation of the cerebral blood supply during gravitational stresses (fig. 96), despite some necessary simplification, provides, in our opinion, a general idea of the processes that maintain the homeostasis of the cerebral circulation at this time and clearly shows that the limits of stability of the system can be increased by broadening the limits of change in the state of the inputs where the mechanisms of compensation are still effective. The material considered in chapter 5 indicates that this can be achieved in several ways, e.g., by change in the functional state of the organism. It can be /200 achieved, above all, by acclimatization to hypoxia.

On the basis of the diagram it is possible to predict what effect latent pathological changes in the cerebrovascular system will have on the resistance of the cerebral circulation to stresses. Under normal conditions these changes may be compensated, but during gravitational stresses they may markedly reduce the permissible limits of the loads. This can be illustrated by comparing the values of two actions P_1 and P_2 (fig. 97) different in force but causing the same impairment of the cerebral blood supply because one of them acts at the normal level, while the other acts against a background of compensated impairment of the cerebral circulation.

Despite the simplification, our diagram focuses attention on some important unresolved matters and suggests the direction of future research on the intracranial circulation as a unique functional system. There are two approaches to the study of this system.

1) The "macroapproach" or construction of a "weak" model. This would include a study of the general characteristics of the system regulating the intracranial circulation without isolating the individual structural elements. In this case the system would be regarded as a "black box." With this approach it would be possible to distinguish the type and general operational features of the system, to determine the precise number of inputs and outputs, to elucidate the quality of regulation, etc. Such an approach also presupposes the elaboration of a mathematical model of the circulatory processes in this sytem, i.e., simulation of the hydrodynamic processes accompanying the flow of blood in the cerebral vessels. The result of this type of research should be the construction of a formal model that takes into account both the characteristics of active regulation of the cerebral blood flow and the hydrodynamic relations in the closed cranial cavity.

2) The "microapproach" or construction of a "strong" model. This would include a study of the structure of the system regulating the intracranial circulation and the interaction of its component parts. It would involve the modeling of these elements in a set of differential equation, a finite-difference scheme or composition of terminal automatic devices. The goal of such an approach would be to ascertain the role of each link in the system regulating the cerebral circulation.

Besides these aspects, it would be of considerable value to investigate the nature of the local regulation of the blood supply in different parts of the brain. Also, it would be worthwhile to study the regulation of the cerebral circulation from the standpoint of comparative physiology. Neither subject has been accorded the attention it deserves. /201

Another matter worth investigating is the response of intracranial circulation to various physical factors. It is also necessary to study the many problems involved in elucidating the mechanisms responsible for impairment of the cerebral circulation in a variety of pathological states of the cerebrovascular system.

Thus, the field of future research on the intracranial circulation is very broad. The use of mathematical modeling, as we tried to show, is quite promising. There will obviously be a need to devise new research techniques for studying the individual parts of the cerebrovascular system which differ from one another in location and in functional characteristics. New methods will have to be devised for investigating and functionally evaluating the cerebral circulation under clinical conditions. And, finally, new methods will have to be developed for processing and analyzing the information obtained.

REFERENCES

1. Avrorov, V. P. 1957. Study of Cerebral Circulation in Chronic Tests Concerning Variations in the Drop Gradient of Arterial Pressure in Vessels Supplying the Brain. Byulleten' Eksperimental'noy Biologii i Meditsiny (Byul. Eksperim. Biol. i Med.), 44, 8, 11-15.
2. Avtandilov, G. G. 1956. The Problem of the Relationship of the Subarachnoid Cavity and the Lymphatic System of the Nasal Cavity. Vestnik Otorinolaringologii (Vestn. Otorinol.), 1, 31-33.
3. Agte, B. S. 1966. Some Controversial Questions of Cranial Rheography. Fiziologicheskiy Zhurnal SSSR imeni I. M. Sechenova (Fiziol. Zh. SSSR), 52, 3, 309-311.
4. Akulinichev, I. T., Bayevskiy, R. M., Zazykin, K. P., and Refreydel', V. 1964. Radioelektronika v kosmicheskoy meditsine (Radio Electronics in Space Medicine), Moscow.
5. Aladzhalova, N. A. 1954. Electrical Constants of the Cerebral Cortex. Doklady Akademii Nauk SSSR (DAN SSSR), 94, 6, 1053-1056.
6. Alov, I. A. 1950. The Question of the Formation of Cerebrospinal Fluid. Byul. Eksperim. Biol. i Med., 29, 2, 238-240.
7. --- 1953. Release Ducts of Cerebrospinal Fluid. Voprosy Neyrokhirurgii (Vopr. Neyrokhirurgii), 4, 19-29.
8. Armstrong, G. J. 1952. Aviation Medicine, Moscow.
9. Anders, E. E. 1899. Report on the Movements of an Exposed Brain. Vrach, 2, 1, 15-16.
10. Arnautov, A. L. 1965. A Portable Transistorized Rheograph. Zhurnal Nevropatologii i Psikhiatrii (Zh. Nevropat. i Psikhiatr.), 65, 10, 1484-1487.
11. Antonov, A. K., Vasilevskiy, N. N., Naumenko, A. I. and Sazonov, S. Ya. 1961. Recording Pulse Pressure and Volume by Tensometry. Fiziol. Zh. SSSR, 47, 2, 275-279.
12. Antoshkina, Ye. D. and Naumenko, A. I. 1960. Changes in Blood Supply to the Cortical Extremities of the Optic and Auditory Analyzers During Stimulation. Fiziol. Zh. SSSR, 46, 11, 1305-1311.
13. Aladzhalova, N. A. and Maslov, N. M. 1957. The Region of Anomalous Dielectric Losses of Skeletal and Smooth Muscles. DAN SSSR, 115, 2, 407-410.
14. Barbashova, Z. I. and Moskalenko, Yu. Ye. 1961. Changes in the Electrical Parameters of the Tissue of Skeletal Musculature as a Result of Acclimation to Hypoxia. Biofizika, 6, 3, 328-330.
15. Babskiy, Ye. B., Vinogradov, T. S., Gurfinkel', V. S., Romel', E. K. and Yakobson, Ya. S. 1952. A New Method for Studying Vascular Reactions in Various Parts of the Body. DAN SSSR, 84, 1, 189-192.
16. Badmayev, K. N. 1958. A Method of Cerebral Oncometry. Byul. Eksperim. Biol. i Med., 46, 11, 118-121.
17. Belekhova, M. G. 1958. Blood Flow in Cerebral Venous Sinuses. Fiziol. Zh. SSSR, 44, 12, 1111-1118.
18. --- 1959. The Nature of Blood Flow in Cerebral Venous Sinuses. Fiziol. Zh. SSSR, 45, 3, 297-303.
19. Belekhova, M. G. and Naumenko, A. I. 1959. Characteristic Pulse Wave Propagation in the Cranial Cavity. Byul. Eksperim. Biol. i Med., 48, 12, 17-20.

20. Benua, N. N., Levin, V. N. and Lesnyan, G. P. 1966. Electroplethysmographic Study of the Blood Volume of the Craniocerebral Cavity, Fiziol. Zh. SSSR, 52, 1, 3-7.
21. Berezin, V. I. 1916. The Effect of Poisons on Cerebral Vessels. Russkiy Vrach, 15, 513-516.
22. Bekhterev, V. M. and Masishchev, V. N. 1928. Associate and Reflex Changes in the Cerebral Pulse. Trudy Gosudarstvennogo Instituta Meditsinskikh Znaniy, 4, 3-29.
23. Blinkov, S. M. and Glezer, I. I. 1964. Mozg cheloveka v tsifrakh i tablitsakh (The Human Brain in Figures and Tables). Leningrad.
24. Blinova, A. M. and Marshak, M. Y. 1963. The Relationship Between Neural and Humoral Mechanisms of the Regulation of Cerebral Circulation. IN: Fiziologicheskiye mekhanizmy regulyatsii mozgovogo krovoobrashcheniya (Physiological Mechanisms for the Regulation of Cerebral Circulation). Leningrad, 3-32.
25. Blinova, A. M. and Ryzhova, N. M. 1958. The Application of the Thermoelectric Method to Study Blood Supply to the Brain in Unanesthetized Dogs. Byul. Eksperim. Biol. i Med., 45, 1, 100-102.
26. --- 1959. Materials on Nervous Regulation of Blood Supply to the Brain. IN: Aktual'nyye Problemy Psikhoterapii, Moscow, 42-51.
27. --- 1961. Nervous Regulation of Blood Supply to the Brain. Vestnik Akademii Meditsinskikh Nauk SSSR (Vestn. AMN SSSR), 5, 56-69.
28. Blyumenau, L. V. 1889. K ucheniyu o davlenii na mozg (Toward the Study of Pressure on the Brain). St. Petersburg.
29. Borishpol'skiy, Ye. S. 1898. Changes in Cerebral Blood Flow During the Horizontal Rotation of Animals. Trudy Kliniki Dushevnykh Bolezney, 1, St. Petersburg.
30. Val'dman, [illegible] A. 1961. Arterial'nyye distonii i distropii (Arterial Dystonia and Dystrophy). Moscow-Leningrad.
31. Vasilevskiy, N. N. and Naumenko, A. I. 1959. Skorost' mozgovogo Krovotoka i Dvizheniye Tserebrospinal'noy Zhidkosti (The Rate of Cerebral Blood Flow and the Motion of Cerebrospinal Fluid). Leningrad.
32. Veyn, A. M. and Ronkin, A. M. 1962. Rheography in the Treatment of Neural Diseases. Zhurnal Nevropatologii i Psikhiatrii, 62, 2, 282-290.
33. Verigo, B. F. 1905. Osnovy fiziologii cheloveka i vysshikh zhivotnykh (Fundamentals of the Physiology of Man and the Higher Animals). 1, St. Petersburg.
34. Vodolazskiy, L. A. 1960. An Electronic Apparatus in Industrial Electrography. IN: Elektronika v Meditsine (Electronics in Medicine), Moscow, 368-373.
35. Volobuyev, Yu. M. 1965. The Question of Cerebral Pulsation in the Human Brain. Zdravookhraneniye Turkmenistana, 10, 20-21.
36. Vokhmyanin, P. F. 1963. The Interrelationship Between Hemodynamic Shifts and Respiration During Accelerations. IN: Aviatsionnaya i kosmicheskaya meditsina (Aviation and Space Medicine). Moscow, 115-118.
37. Gazenko, O. G., Chernigovskiy, V. N. and Yazdovskiy, V. I. 1964. Biological and Physiological Studies During Flights in Rockets and Artifical Earth Satellites. IN: Problemy Kosmicheskoy Biologii (Problems of Space Biology), Moscow, 3, 23-37.
38. Gal'perin, M. P. 1960. Antografiya golovnogo mozga (Cerebral Antography). Leningrad.

39. Gamayunov, S. F. 1927. The Effect of a Lack of Nasal Respiration on Cerebral Vessels. Vestnik Rinolyaringootiatrii, 5, 589-594.
40. Gilyarovskiy, V. A., Liventsev, N. M., Segal', Yu. G. and Kiriyalova, Z. A. 1953. Elektroson (Electrosleep). Moscow.
41. Gindtse, V. K. 1947. Arterial'naya sistema golovnogo mozga cheloveka i zhivotnykh (The Arterial System of the Brain in Man and Animals). Moscow.
42. Glushkov, V. M. 1962. Sintez tsifrovykh avtomatov (Synthesis of Numerical Automata). Moscow.
43. Golland, E. B. 1960. Cerebral Piezopulsography in Cerebral Arteriosclerosis and Hypertonic Disease in the Sclerotic Phase. Zhurnal Nevropatologii i Psikhiatrii, 15, 6, 672-678.
44. Gorev, V. P. 1947. Tests and Future Application of the Tarkhanov Phenomenon in Clinical Practice. IN: Trudy VII S"yezda Fiziol., Biokh. i Farmakol., Moscow, 643-645.
45. Granat, L. N. and Moskalenko, Yu. Ye. 1965. Changes in the Hemodynamics of the Human Mammary Gland During Hot and Cold Stimuli. Fiziol. Zh. SSSR, 51, 9, 1100-1107.
46. Grigorenko, N. P. 1960. Application of the Topographic Method to Study of the Human Cerebral Vessels. Trudy Volgogradskogo Oblastnogo Onkodispansera, 3, 242-297.
47. Gyurdzhian, A. A., Laneva, M. A. and Radkovich, L. A. 1963. Content of Nonesterified Fatty Acids in the Plasma of Rats Exposed to Accelerations. DAN SSSR, 151, 5, 982-985.
48. Davydov, V. G. 1941. Changes in the Electrical Resistance and Polarization of the Skin Under the Action of Heat. IN: Tezisy Dokladov Sessii Moskovskogo Obshchestva Fiziologov, Biokhimikov i Farmakologov (Abstracts of Reports from the Session of the Moscow Society of Physiologists, Biochemists and Pharmacologists). Moscow, 76.
49. Yegorova, V. V. 1958. Innervation of the Venous Sinuses of the Human Dura Mater. Trudy Kubanskogo Meditsinskogo Instituta, 16, 1-6.
50. Zhukov, N. A. 1895. Toward the Problem of the Effect of a Cessation of Cerebral Circulation on Cortical Excitability. Bol'nichnaya Gazeta Botkina, St. Petersburg, 1086-1092.
51. Zavarzin, A. A. and Shchelkunov, S. A. 1954. Rukovodstvo po Gistologii (Textbook on Histology). Leningrad.
52. Zlatoverov, A. N. 1955. The Mechanism of Increasing Intracranial Pressure. Voprosy Neyrokhirurgii, 6, 3-8.
53. Zolotarov, A. I. 1964. The Problem of Electronic Modelling of the Circulatory System. IN: Elektronika i khimiya v kardiologii (Electronics & Chemistry in Cardiology). Voronezh, 179-185.
54. Ivanov, G. F. 1935. The Movement of Cerebrospinal Fluid in the Brain and in its Subdural Spaces. Arkhivy Biologicheskikh Nauk, 39, 1, 5-49.
55. --- 1955. Ducts for the Flow of Cerebrospinal Fluid. Trudy Nauchno-issledovatel'skogo Instituta Ukha, Gorla, Nosa, 6, 309-314.
56. Izmaylova, I. V. 1957. Angioarchitechtonics of the Human Cerebral Cortex. Arkhivy Anat. Gistol. i Embriol., 34, 6, 38-44.
57. Kas'yan, I. I. 1963. Reaction of the Cardiovascular and Respiratory Systems of Animals in the Air-tight Cabins of Rockets at Altitudes of up to 212 km. Izvestiya Akademii Nauk SSSR (Izv. AN SSSR), Seriya Biologiya, 1, 24-39.

58. Kedrov, A. A. 1941. A New Method for Determining the Pulse Fluctuations of Blood Volume in Vessels of Various Parts of the Human Body. Klinecheskaya Meditsina, 19, 1, 71-81.
59. Kedrov, A. A. and Naumenko, A. I. 1954. Voprosy fiziologii vnutricherepnogo krovoobrashcheniya s klinicheskim ikh osveshcheniyem (Questions of the Physiology of Intracranial Circulation and their Clinical Ramifications). Leningrad.
60. Kedrov, A. A., Naumenko, A. I. and Degtyareva, Z. Ya. 1954. The Mechanism of the Venous Flow of Blood from the Brain. Byul. Eksperim. Biol. i Med., 35, 9, 10-14.
61. Kiselev, A. A. 1962. Some Peculiarities of the Hemodynamics and Gas-Exchange in a Limited Cycle of Blood Circulation During Transverse Accelerations. IN: Problemy Kosmicheskoy Biologii (Problems of Space Biology), 2, 231-236.
62. Klimovitskiy, V. Ya. 1963. The Effect of Centrifugal Accelerations on the Venous Flow in Cerebral Vessels of Animals. IN: Aviatsionnaya i Kosmicheskaya Meditsina (Aviation and Space Medicine), Moscow, 250-251.
63. Klosovskiy, B. N. 1942. The Present State of the Problem of Blood Circulation in the Brain and the Vasodilatory Effect on Cerebral Vessels. Voprosy Neyrokhirurgii, 6, 49-60.
64. --- 1951. Tsirkulyatsiya krovi v mozgu (Blood Circulation in the Brain). Moscow.
65. Klosovskiy, B. N. and Kosmarskaya, Ye. N. 1961. Deyatel'noye i tormoznoye sostoyaniye mozga (The Active and Inhibitory State of the Brain). Moscow.
66. Kovalenko, Ye. A. 1961. A Method for Continuous Recording of Oxygen Tension in the Brain of a Dog Under Conditions of Low Barometric Pressure. Patologicheskaya Fiziologiya i Eksperimental'naya Terapiya (Patol. Fiziol. i Eksperim. Terapiya), 5, 2, 66-70.
67. Kovalenko, Ye. A. 1962. The Effect of a High Degree of Atmospheric Rarefaction on Oxygen Tension in Brain Cells. Fiziol. Zh. SSSR, 48, 2, 150-158.
68. Komendantov, L. Ye. 1927. The Effect of the Character of Respiration on Intracranial Pressure. Vestnik Rino-lyaringo-Otiarii, Rostov on the Don, 2, 174-180.
69. Konovalova, M. K., Perli, P. D. and Moskalenko, Yu. Ye. 1961. The Possibility of Studying Cerebral Circulation in Man by Rheography. IN: Voprosy Morfologii i Fiziologii, Riga, 137-140.
70. Konstantinovskiy, G. A. 1960. The Question of Innervation of the Pia Mater. Arkhivy Anatomii, Gistologii i Embriologii, 39, 11, 97-101.
71. Konradi, G. P. and Parolla, D. I. 1963. Blood Supply to the Brain in its Various Functional States. IN: Works of the Symposium "Fiziologicheskiye mekhanizmy regulyatsii mozgovogo krovoobrashcheniya (Physiological Mechanisms of the Regulation of Cerebral Circulation)". Leningrad, 72-120.
72. Kopylov, M. B. 1947. X-ray Representation of the Venous Circulation in the Cranium. DAN SSSR, 18, 6, 1231-1232.
73. --- 1965. Some Examples of the Automatic Control of Cerebral Hemodynamics and Calcium Exchange in Cranial Tissues. IN: Bionika (Bionics), Leningrad, 396-401.

74. Kotel'nikov, Ye. A. 1962. Direct Massage of the Heart in Terminal Conditions and Changes in Cerebral Circulation Thereof. IN: Trudy Oblastnogo S"yezda Khirurgov (Works of the Oblast Conference of Surgeons), Voronezh, 125-129.
75. Kotovskaya, A. R. and Yuganov, Ye. M. 1962. The Effect of Prolonged Transverse Accelerations on the Organism of Animals. IN: Problemy Kosmicheskoy Biologii (Problems of Space Biology), 1, 384-392.
76. Lebedev, F. M., Fitzon-Ryss, Yu. I. and Kolesnikov, A. I. 1964. The Problem of the Rate of Pulse-Wave Propagation. Kardiologiya, 4, 3, 82-87.
77. Liberman, G. Yu. 1958. A Method of Studying Fluctuations of Cerebral Vascular Tonus in Experiments on Animals. Byul. Eksperim. Biol. i Med., 45, 1, 111-114.
78. Marshak, M. Ye. 1963. A Thermoelectric Method of Studying Regional Circulation in Acute and Chronic Experiments. Sovremennyye Metody Issledovaniya Funktsii Serdechno-Sosudistoy Sistemy (Modern Methods in the Study of Functions of the Cardiovascular System), Moscow, 101-108.
79. Medvedev, V. P. 1964. A Method of Determining the Rate of Pulse-Wave Propagation. Kardiologiya, 4, 1, 79-82.
80. Mikhaylov, S. S. 1965. Arterio-venoznyye sonno-peshcheristyye anevrizmy (Arterio-Venous Carotid-Cavernous Aneurism). Moscow.
81. --- 1966. A Model of a Circulatory-Isolated Dog's Head and Isolated Sinocarotid Zone with Chiasmic Blood Supply for a Study of Cerebral Circulation. Fiziol. Zh. SSSR, 52, 2, 201-204.
82. Mishchuk, N. N. 1948. A Method of Electrically Investigating Perspiration and Tests of its Experimental and Clinical Application. Leningrad.
83. Moskalenko, Yu. Ye. 1958. Application of Superhigh Frequencies for Biological Investigations, Biofizika, 3, 5, 619-626.
84. --- 1959. Mechanical Photoelectric Converters. Fiziol. Zh. SSSR, 45, 7, 883-886.
85. --- 1961. Cerebral Pulsation in the Hermetic Cavity of the Brain. Izv. AN SSSR, Ser. Biol., 4, 620-629.
86. --- 1962a. The Possibility of an Experimental Evaluation of Blood Supply to the Brain Under Conditions of an Altered Gravitational Field. IN: Problemy Kosmicheskoy Biologii (Problems of Space Biology), 2, 407-415.
87. --- 1962b. Optimal Conditions for Recording Electroplethysmograms of Parts of the Human Body and its Organs. Fiziol. Zh. SSSR, 48, 2, 214-218.
88. --- 1964. Telemetric Equipment for Studying Blood Circulation of the Brain. J. Physiology, 172, 3-4.
89. Moskalenko, Yu. Ye., Bayevskiy, R. M. and Gazenko, O. G. 1962. A Method for Studying Cerebral Circulation under Conditions of an Altered Gravitational Field. IN: Problemy Kosmicheskoy Biologii (Problems of Space Biology), 1, 401-407.
90. Moskalenko, Yu. Ye., Benua, N. N. and Graunov, O. V. 1963. The Dynamics of Blood Supply to the Brain During Changes in Directions of a Gravitational Field. Fiziol. Zh. SSSR, 405-411.
91. Moskalenko, Yu. Ye., Gazenko, O. G., Shurubura, A. A., Kas'yan, I. I. and Graunov, O. V. 1964a. The Dynamics of Hemocirculatory Parameters of the Cerebral Vascular System During Longitudinal Accelerations. Izv. AN SSSR, Ser. Biol., 2, 280-297.

92. Moskalenko, Yu. Ye., Graunov, O. V., Gazenko, O. G. and Kas'yan, I. I. 1964b. The Reaction of the Vascular System of the Craniocerebral Cavity During Equivalent Longitudinal Gravitational Overloads of ± 1 Unit. IN: Problemy Kosmicheskoy Biologii (Problems of Space Biology), 3, 366-378.
93. Moskalenko, Yu. Ye., Cooper, R., Crow, H. and Walter, W. G. 1964c. Variation in Blood Volume and Oxygen Availability in the Human Brain. Nature, 202, 4928, 159-161.
94. Moskalenko, Yu. Ye. and Naumenko, A. I. 1956. The Theory of the Method of Electroplethysmography. Fiziol. Zh. SSSR, 42, 3, 312-316.
95. --- 1957. Fluctuations in the Movement of the Cerebrospinal Fluid in the Cerebral Cavity and Spinal Cord. Fiziol. Zh. SSSR, 43, 10, 928-933.
96. --- 1959a. Study of the Character of Cerebrospinal Fluid Displacement in Normal Animals. Fiziol. Zh. SSSR, 45, 5, 562-568.
97. --- 1959b. Variations in the Electroconductivity of the Blood During Movements. Byul. Eksperim. Biol. i Med., 50, 2, 77-82.
98. --- 1964. Hemodynamics of Cerebral Circulation. IN: Cerebral Ischemia, Springfield, 21-61.
99. Mchedlishvili, G. I. 1959. The Study of Localization of "Closing Mechanisms" in Regional Arteries of the Brain (Internal Carotid and Vertebral Arteries). DAN SSSR, 124, 6, 1371-1374.
100. --- 1962. The "Thorax-Head" Preparation for Study of Cerebral Circulation. Byul. Eksperim. Biol. i Med., 53, 2, 123-125.
101. --- 1966. Funktsii sosudistykh mekhanizmov golovnogo mozga (The Functions of the Vascular Mechanisms of the Brain). Tiflis, Manuscript.
102. Mchedlishvili, G. I., Akhobadze, V. A. and Ormotsadze, L. G. 1962. Hemodynamic Mechanisms of Compensation of Cerebral Circulation Under Conditions of Temporary Occlusion of the Cranial Vena Cava. Fiziol. Zh. SSSR, 48, 6, 684-691.
103. Mchedlishvili, G. I. and Ormotsadze, L. G. 1963. Study of Reflex Influences from Venous Sinuses to Regional Arteries of the Brain. Byul. Eksperim. Biol. i Med., 53, 2, 9-13.
104. Navalikhin, I. 1874. Napryazheniye mozga i yego vzaimnyye sootnosheniya s krovoobrashcheniyem (Cerebral Tension and its Interrelationships with Circulation). Kazan.
105. Nagel', K. K. 1889. O kolebaniyakh kolichestva krovi v golovnom mozgu pri razlichnykh usloviyakh (Fluctuations in Blood Volume in the Brain Under Various Conditions). Moscow.
106. Nadareyshvili, K. Sh. 1962. Fluctuations of the Tonus of Regional Arteries of the Brain Synchronized with Respiration. IN: Sovremennyye Problemy Morfologii, Fiziologii i Patologii (Modern Problems in Morphology, Physiology and Pathology). Tiflis, 135-142.
107. Nadzharyan, N. A. 1948. The Effect of Stimulation of the Auditory, Olfactory and Visual Exteroreceptive Systems on the Performance of Human Craniocerebral Vessels. Vestn. Otorinol., 1, 14-18.
108. Naumenko, A. I. 1956. Fluctuations of Pressure in the Hermetically Sealed Cranial Cavity. Fiziol. Zh. SSSR, 42, 8, 660-667.
109. --- 1957. Recording Intracranial and Arterial Pressures Using Direct Piezography. Fiziol. Zh. SSSR, 43, 4, 366-370.

110. Naumenko, A. I., Antonov, A. K., Moskalenko, Yu. Ye. and Sazonov, S. Ya. 1962. New Data on the Mechanism of Intracranial Circulation. Fiziol. Zh. SSSR, 48, 10, 1253-1259.
111. Naumenko, A. I. and Vasilevskiy, N. N. 1962. The Relationship Between Pulse and Tonus of Cerebral Vessels. Byul. Eksperim. Biol. i. Med., 54, 8, 12-16.
112. Naumenko, A. I. and Olisov, V. S. 1959. The Effect of Stimulation of the Vestibular Analyzer on Cerebral Circulation. Trudy V S"yezda Otorinol. SSSR (Works of the Fifth Conference of Otorhinologists of the USSR), 7-12 July 1958, Leningrad, 117-178.
113. Novik, I. B. 1965. O modelirovanii slozhnykh sistem (Modeling Complex Systems), Moscow.
114. Orlov, V. V. 1961. Pletizmografiya (Plethysmography). Leningrad.
115. Pavlovskiy, Ye. N. 1948. The Problem of the Regulation of Blood Circulation in the Head. Trudy Kazanskogo Nauchno-issledovatel'skogo Veterinarnogo Instituta. 10, 124-142.
116. Parolla, D. I. 1959. Various Reflexes of Cerebral Vessels According to Thermoencephalographic Data in Acute and Chronic Tests. Nauchnyye Soobshcheniya Instituta Fiziologii imeni I. P. Pavlova, 1, 135-137.
117. Perlin, B. Z. 1955. The Receptor Apparatus of the Cerebral Dura Mater. IN: Tezisy Dokladov Nauchnoy Sessii, Posvyashennaya 10-letiyu Kishinevskogo Gosudarstvennogo Meditsinskogo Instituta (Abstracts of Reports of the Scientific Session Dedicated to the Tenth Anniversary of the Kishinev State Medical Institute). Kishinev, 27-28.
118. Pirogov, N. I. 1864. Nachala Obshchey Voyenno-Polevoy Khirurgii (Principles of General Military Field Surgery). Moscow-Leningrad, 1941.
119. Polyakov, G. I. 1949. Structural Organization of the Human Cerebral Cortex According to Data on its Development During Ontogenesis. IN: Tsitoarkhitektonika kory bol'shogo mozga cheloveka (Cytoarchitechtonics of the Human Cerebral Cortex). Moscow, 33-91.
120. Pravdich-Neminksiy, V. V. 1950. Pulse Fluctuations and Rates of Their Propagation Through the Human Arterial Vessels, DAN SSSR, 75, 3, 461-464.
121. Prives, M. G. 1963. The Effect of Accelerations on the Structure of the Vascular System. Arkh. Anat., Gistol. i Embriol., 11, 3-13.
122. Ragozin, L. and Mendel'son, M. 1880. Graphische Untersuchungen über die Bewegungen des Gehirns beim lebenden Menschen. Graphic Investigation of Movement of the Brain in Live Humans. St. Petersburg, Med. Zh., 37, 303-304.
123. Reznikov, M. and Davidenkov, S. 1911. Beiträge zur Plethysmographi des Menschlichen Gehirns. Plethysmography of the Human Brain. Zh. Neyrol. i Psikhiat., 4, 129-193.
124. Ryvlina, Kh. S. 1941. Electroconductivity of the Skin as a Method of Studying Reactions of Children to Meteorological Factors. IN: Tezisy dokladov 1-oy Sessii Moskovskogo Obshchestva Fiziologov, Biokhimikov i Farmakologov (Abstracts of Reports of the First Session of the Moscow Society of Physiologists, Biochemists and Pharamcologists). Moscow, 205.
125. Savitskiy, N. N. 1956. Nekotoryye metody issledovaniya i funktsional'noy otsenki sistemy krovoobrashcheniya (Some Methods of Study and Functional Analysis of the Circulatory System). Leningrad.

126. Sakhnovskaya, A. A. 1919. Problem of the Effect of Pharmacological Preparations on the Vessels of an Isolated Cerebrum. Izvestiya Komissariata Zdravookhraneniya, May-December, Pgr., 7-12.
127. Sepp, Ye. K. 1926. Klinicheskiy analiz nervnykh bolezney. Narusheniye krovoobrashcheniya (Clinical Analysis of Nervous Diseases. Circulatory Disorders). Moscow-Leningrad.
128. Sepp, Ye. K. 1928. Die Dynamik der Blutzirkulation im Gehirn (The Dynamics of Blood Circulation in the Brain). Berlin.
129. Skokovskiy, N. I. 1856. Movement of the Brain. Voyenno-Meditsinskiy Zhurnal, 67, 9, 11-13.
130. Snezhko, A. D. 1956. Determination of the Concentration of Unbound Oxygen in Cerebral Tissue Under Conditions of Chronic Examination. Biofizika, 1, 6, 585-592.
131. Sokolov, S. P. and Pukhidskiy, A. K. 1932. An Attempt at Experimental Study of the Dynamics of the Spinocerebral Fluid. Permsk, Meditsinskiy Zhurnal, 3-4, 35-42.
132. Spirov, M. S. 1927. The Subarachnoid Space of the Brain and Spinal Column and its Relationship to the Spinocerebral Fluid. Russk. Arkh. Anat. Gistol. i Embriol., 6, 2, 269-280.
133. Sreseli, M. A. and Bol'shakov, O. P. 1962. The Significance of the Sinus Cavernosa in the Regulation of Cerebral Circulation. Arkh. Anat., Gistol. i Embriol., 43, 10, 13-18.
134. Ugryumov, V. I., Suponitskaya, M. A., Shekhter, S. Ye., Mityashin, P. P. and Maksimov, V. P. 1957. A New Method for Measuring Fluid Pressure. Voprosy Neyrokhirurgii, 3, 52-55.
135. Umanskiy, K. G. 1957. New Methods of Studying Vascular Reactions in the Brain. IN: Aktual'nyye Problemy Nevropatologii i Psikhiatrii (Current Problems in Neuropathology and Psychiatry). Kuybyshev, 69-75.
136. Filanovskaya, T. P. 1966. The Occurence of the Anomalous Dispersion of Dielectric Parameters of Living Tissue in the Low Radio Frequency Range. Biofizika, 11, 2, 276-280.
137. Fridman, A. P. 1957. Osnovy likvorologii (Ucheniye o zhidkosti mozga) (Fundamentals of Studying Fluids(Study of Brain Fluids)). Leningrad.
138. Khazen, I. M. and Vaysfel'd, I. L. 1962. Variations in the Content of Biologically Active Substances in Rats Under the Influence of Radial Accelerations. Voprosy Meditsinskoy Khimii, 8, 5, 493-497.
139. Khodyakov, N. P. 1927. The Effect of the Character of Respiration on the Movement of Cerebrospinal Fluid. Vestn. Rino-lyaringootiatrii, 3-4, 359-363.
140. Shamburov, P. A. 1954. Spinnomozgovaya Zhidkost' (The Cerebrospinal Fluid). Moscow.
141. Shul'zhenko, Ye. B. 1965. Peculiarities of the Reflex Regulation of Hemodynamic Shifts Under the Action of Transversely Directed Accelerations. Byul. Eksperim. Biol. i Med., 60, 10, 36-38.
142. Shurubura, A. A., Barbashova, Z. A. and Moskalenko, Yu. Ye. 1965. Intracranial Blood Volume During Accelerations in Rats Acclimated to Hypoxia. Fiziol. Zh. SSSR, 51, 12, 1474-1477.
143. Zninya, G. I. 1962. Cranial Rheography During Various Vascular Diseases. Klinicheskaya Meditsina, 9, 89-94.
144. --- 1965. The Problem of the Method of Cranial Rheography. Materialy nauchnoy konferentsii po voprosam serdechnososudistoy patologii (Materials

from the Scientific Conference on Problems of Cardio-vascular Pathology). Riga, 67-68.
145. Entina, I. D. and Yakovlev, V. A. 1951. A Method of Studying Oxidation Processes in Cerebral Tissues. Biokhimiya, 16, 6, 567-571.
146. Yunusov, A. 1937. Conditioned-Reflex Perspiration in Man. Fiziol. Zh. SSSR, 23, 3, 381-384.
147. Yanovskiy, M. V. 1922. Kurs diagnostiki (Course in Diagnostics).
148. Yazdovskiy, V. I. 1964. Basic Scientific Trends in Space Biology and the Conquest of Space. IN: Problemy Kosmicheskoy Biologii (Problems of Space Biology), 3, 5-9.
149. Yarullin, Kh. Kh. The Problem of Diagnosing the Pathological Convolution of Carotid Arteries using Rheoencephalography. Zhurnal Nevropatologii i Psikhiatrii, 65, 10, 1476-1483.
150. Ackermann, Th. 1858. Untersuchungen über den Einfluss Ertichung auf die Menge des Blutes im Gehirn und in den Lungen (Research on the Effect of Posture on the Amount of Blood in the Brain and Lungs). Virch. Arch., 15, 401-464.
151. Adey, W. R., French, J. D., Kado, R. T., Lindsley, D. F., Walter, P. O., Wendt, R. and Winters, W. D. 1964. EEG Records from Cortical and Deep-Brain Structures During Centrifugal and Vibrational Accelerations in Cats and Monkeys. IRE Trans. Bio-Med. Electron., 8, 3, 182-188.
152. Ahrens, H. 1913. Experimentelle Untersuchungen über die Stromung des Liquor cerebrospinalis. (Experimental Research on the Flow of the Cerebrospinal Fluid). Z. ges. Neurol. u. Psychiat., 15, 578-593.
153. Albrecht, H. 1921. Die umschriebene Herabsetzung der Gleichstromwiderstandes der menschlichen Haut bei gynäkologischen Neurosen. (Circumscribed Reduction of Direct Current Resistance of the Human Skin in Gynecological Neuroses). Leipzig.
154. Avman, N., Bering, E. A. 1961. Plastic Model for the Study of Pressure Changes in the Circle of Willis and Major Cerebral Arteries Following Arterial Occulusion. J. Neurosurg., 18, 361-366.
155. Bakay, L. 1941. Die Innervation der Pia mater, der Plexus chorioidei und der Hirngefässe. (Innervation of the Pia Mater, Plexus Choriodei and Blood Vessels of the Brain). Arch. Psychiat. u Nervenkranheit., 113, 2, 3, 412-427.
156. Baldwin, B. A. and Bell, F. R. 1963. Blood Flow in the Carotid and Vertebral Arteries of the Sheep and Calf. J. Physiol., 167, 448-462.
157. Banchero, N., Cronin, L., Nolan, A. C. and Wood, E. H. 1965. Blood Oxygen Changes Induced by Forward (+6) Acceleration. Aerospace Med., 36, 7, 608-629.
158. Barnett, C. H. and Marsden, C. D. 1961. Functions of the Mammalian Carotid Rete Mirabile. Nature, 191, 4783, 88, 89.
159. Becher, E. 1922. Untersuchungen über die Dynamik des Liquor cerebrospinalis. (Research on the Dynamics of the Cerebrospinal Fluid). Mitteil. Grenzgeb. Med. u. Chir., 35, 366-388.
160. Beckman, E. 1956. The Influence of Footward Acceleration Upon the Fluid Systems of Intracranial Cavity. Physiol. Rev., 36, Suppl. 2, 10-14
161. Bedford, T. H. 1935. Effect of Increased Venous Pressure on the Pressure of Cerebrospinal Fluid. Brain. 58, 427-447.
162. Bedford, T. H. 1955. The Movement of Cerebrospinal Fluid From the Subarachnoid Space of the Dog. J. Physiol., 128, 2, 51-52.

163. Beer, O., Schlegel, H. and Schley, W. 1956. Die Messung durchblutungsabhangiger Scheinleitwertsönderrunger im menschlicher Schädel. (Measurement of Circulation-Dependent Changes of Admittance in the Human Cranium). Naturwissenschaften, 43, 3, 49-51.
164. Beier, W. 1960. Biophysik (Biophysics). Leipzig.
165. Bering, E. A. 1955. Chorioid Plexus and Arterial Pulsation of Cerebrospinal Fluid. Arch. Neurol. and Psychiat., 73, 2, 165-172.
166. Bernsmeier, A. U. and Siemons, K. 1953. Die Messung der Hirndurchblutung mit der Stickoxydul Methode (Measurement of Blood Circulation in the Brain by the Nitrous Oxide Method). Pflüg. Arch., 258, 149-162.
167. Berthold, H. 1869. Zur Blutcirculation in geschlossenen Höhlen (Blood Circulation in Closed Cavities). Zbl. med. Wiss., 43, 673-675.
168. Betz, E. 1965. Zur Registrierung der lokelen Gehirndurchblutung mit Warmeleitsonteden. (Recording of Local Cerebral Blood Circulation with Heat-Conducting Probes). Pflüg. Arch., 284, 3, 278-284.
169. Biedl, A. and Reiner, M. 1900. Studien über Hirncirculation und Hirnödem. (Studies on Brain Circulation and Brain Edema). Pflüg. Arch., 79, 158-194.
170. Bowsher, D. 1953. The Cerebrospinal Fluid Pressure. Brit. Med. J., 15, 45, 863-865.
171. Bowsher, D. 1957. Pathways of Absorption of Protein From the Cerebrospinal Fluid: An Autoradiographic Study in the Cat. Anat. Rec., 128, 1, 23-39.
172. Bowsher, D. 1958. Further Considerations of Cerebrospinal Fluid Dynamics. Brit. Med. J., 19, 917-919.
173. --- 1960. Cerebrospinal Fluid Dynamics in Health and Disease. Springfield.
174. Bradbury, N. W. B., Davson, H. and Lathem, W. 1964. A Flow of Cerebrospinal Fluid Along the Central Canal of the Spinal Cord of the Rabbit. J. Physiol., 172, 17p-19p.
175. Brain, S. R. 1957. Order and Disorder in the Cerebral Circulation. Lancet, 7001, 857-862.
176. Browne, M. K. and Fitzsimons, J. T. 1959. Electrocardiographic Changes During Positive Acceleration. Brit. Heart J., 21, 1, 23-30.
177. Clark, M. E., Martin, I. D., Wenglarz, R. A., Knapp, F. M. and Himwich, W. A. 1965. Engineering Analysis of the Hemodynamics of the Circle of Willis. Arch. Neurel., 13, 2, 173-183.
178. Collan, F. and Namon, R. 1965. Experimental Analysis of the Rheoencephalogram (REG). Proc. Soc. Exptl. Biol. and Med., 118, 3, 809-811.
179. Cooper, R. 1963. Local Changes of Intracerebral Blood Flow and Oxygen in Humans. Med. Electron. Biol. Engng., 1, 3, 529-536.
180. Cooper, R., Moskalenko, Yn. and Walter, W. 1964. Pulsation of the Human Brain. J. Physiol., 172, 52p-56p.
181. Craigie, E. H. 1945. The Architecture of the Cerebral Capillary Bed. Biol. Rev., 20, 4, 133-146.
182. Cramer, P. 1873. Experimentelle Untersuchungen über den Blutdruck in Gehirn. (Experiments on Blood Pressure in the Brain. Inaugural Dissertation, Janang. Diss., Dorpat.
183. Critchley, M. 1930. The Anterior Cerebral Artery and its Syndromes. Brain. 53, 4, 120, 166.

184. Cropp, G. I. A. and Burton, A. C. 1966. Theoretical Considerations and Model Experiments on the Validity of Indicator Dilution Methods for Measurements of Variable Flow. Circulat. Res., 18, 1, 26-48.
185. Cross, B. A. and Silver, I. A. 1962. Some Factors Affecting Oxygen Tension in the Brain and Other Organs. Proc. Roy. Soc. Biol., 156, 483-499.
186. Crow, H. J., Cooper, R. and Phillips, D. G. 1961. Controlled Multifocal Frontal Leucotomy for Psychiatric Illness. J. Neurol., Neurosurg., Psychiat., 24, 353-360.
187. Curtis, I. 1949. Rapid Serial Angiography Preliminary Report. J. Neurol., Neurosurg., Psychiat., 12, 3, 167-181.
188. Denison, A. B., Spencer, M. P. and Green, H. D. 1955. A Squarewave Electromagnetic Flowmeter for Application to Intact Blood Vessels. Circulat. Res., 3, 1, 39-46.
189. Dermiksian, G. 1960. The Problem of Loss of Consciousness in Flying Personnel. Amer. J. Cardiol., 6, 1, 45-53.
190. Dewar, H. A., Owen, S. G. and Lenkins, A. R. 1953. Influence of Tolozoline Hydrocloride (Priscol) on Cerebral Blood Flow. Lancet, 264, 867-869.
191. Dixon, W. E. and Halliburton, W. D. 1916. The Cerebrospinal Fluid. IV. J. Physiol., 3, 198-217.
192. Donders, F. C. 1851. Die Bewegungen des Gehirns und die Veränderungen der Gefässfüllung der Pia mater auch bei geschlossenem unausdehnbarem, Schädel unmittelbar beobachtet. (Motions of the Brain and Changes in the Filling of Blood Vessels of the Pia Mater, Directly Observed in the Case of Closed Inexpandible Cranium (Review)). Ref. Schmidt's Jahrb., 69, 16-20.
193. Donzelot, E., Meyer-Heine, A., Milovanovich, J. B. and Dreyfus, B. 1951. L'étude de la circulation cerebrale par la diagraphie. (Study of Cerebral Circulation by Diagraphy). Societe française de cardiologie, 17 Dec. 1950, Presse mrd., 59, 17, 339.
194. Dumarco, K. and Rimini, R. 1947. Dumarco La presión del liquido cefalorachideo y las presión de las venas yugalares. (The Pressure of the Cerebrospinal Fluid and the Pressure of the Jugular Veins). Rev. grent de Cariol., 14, 4, 239-359.
195. Dumke, P. R. and Dumke, C. F. 1941. Measurement of Total Cerebral Blood Flow in the Monkey. Amer. J. Physiol., 133, 2, 266-268.
196. Duvoisin, R. C., Kruse, F. Ir. and Saunders, D. 1962. Convulsive Syncope Induced by the Valsalva Maneuver in Subject Exhibiting low "G" tolerance. Aerospace Med., 33, 1, 92-96.
197. Ecker, A. 1844. Physiologische Untersuchungen über die Bewegung des Gehirns und Rückenmarks insbesondere den Einfluss der Cerebrospinalflussigkeit auf dieselben (Ref.) (Physiological Studies Concerning Motion of the Brain and Spinal Cord, Particularly the Effect of the Cerebrospinal Fluid Thereon (Review)). Schmidts jahrb., 44, 240-243.
198. Eichorn, O. 1959. Die Kardiocirculographie-eine klinische Methode zur Messung der Hirndurchblutung (Cardiocirculography: A Clinical Method for Measurement of Cerebral Circulation). Wien. Klin. Wschr., 71, 28, 499-502.
199. Erbslöh, H. 1955. In: Deutung und Fehlerdeutung von Durchblutungsstörungen des Gehirns (In: Interpretation and Evaluation of Error in Disturbances of the Cerebral Blood Circulation. Congress of German Internists). Dtsch. Internisten-Tagung. Leipzig., 120-132.

200. Ewig, W. and Lullies, H. 1924. Der Einfluss der Atmung auf die Druckschwankungen in Cerebrospinalkanal (Effect of Respiration on the Variations of Pressure in the Cerebrospinal Canal). Z. exptl. Med., 43, 764-781.
201. Falkenheim, H. and Naunyn, B. 1887. Über Hirndruck (Cerebral Pressure). Arch. Pathol. u. Pharmacol., 22, 261-305.
202. Fejfar, Z. and Zajitz, F. 1955. Vyhledy impedanini plethysmografie pro kliniku (Prospect of Impedance Plethysmography for the Clinic). Casopisi lekarii. Clesk., 94, 252-254.
203. Feryglio, F. S. 1954. La circolazione cerebrale (Cerebral Circulation). Omnia medika, 32, 5-6, 337-380.
204. Fleisch, A. 1927. Der normall Blutdruck. Handbuch norm. u. path. (Normal Blood Pressure). Physiol., 7, 2, 1295-1303.
205. Flexner, L. B., Clark, J. H. and Weed, L. H. 1932. The Elasticity of the Dural Sac and its Contents. Amer. J. Physiol., 101, 2, 292-304.
206. Fog, M. 1938. The Relationship Between the Blood Pressure and the Tonic Regulation of the Pial Arteries. J. Neurol. and Psychiat., 1, 187-197.
207. Folkow, S. 1956. Control of the Circulation of the Blood. London.
208. Forbes, H. S., Nason, H. T. and Wortman, R. C. 1937. Cerebral Circulation, Vasodilatation in Pia Following Stimulation of Vagus, Aortic and Carotid Sinus Nerves. Arch. Neurol. and Psychiat., 37, 334-351.
209. Forbes, H. S. and Cobb, S. S. 1938. Motor Control of Cerebral Vessels. Brain. 60, 221-233.
210. Frazier, C. H. and Peet, M. M. 1914. Factors of Influence on the Origin and Circulation of the Cerebrospinal Fluid. Amer. J. Physiol., 35, 3, 268-283.
211. Gardner, W. J. 1946. Cerebrospinal Fluid Dynamics. Medical Physics, 1, 148-152.
212. Gauer, O. H. and Henry, J. P. 1964. Negative Acceleration in Relation to Arterial Oxygen Saturation, Subendocardial Hemorrhage and Venous Pressure in the Forehead. Aerospace Med., 34, 6, 533-545.
213. Geigel, R. 1905. Die Rolle des Liquor Cerebrospinalis bei der Circulation im Schädel (Role of the Cerebrospinal Fluid on Intracranial Circulation). Pflüg. Arch., 109, 337-354.
214. Gibbs, F. A. 1933. A Thermo-electric Blood Flow Recorder in the Form of a Needle. Proc. Soc. Exptl. Biol. and Med., 31, 141-146.
215. Gibbs, F., Lennox, W. G. and Gibbs, E. 1934. Cerebral Blood Flow Preceding and Accompnaying Epileptic Seizures in Man. Arch. Neurol. and Psychiat., 32, 2, 257-272.
216. Gilland, O. 1965. CSF Dynamic Diagnosis of Spinal Block. Acta Neurol. Scand., 41, 5, 487-496.
217. Grashey, H. 1892. Experimentalle Beiträge zur Lehre von der Blutcirculation in der Schädel-Rückgratshöhle (Experimental Contribution to the Knowledge of Intracranial Blood Circulation). München.
218. Graveline, R. and Cally, M. 1962. Body Fluid Distribution: Implication for Zero Gravity. Aerospace Med., 33, 11, 1281-1290.
219. Greits, T. 1956. A Radiologic Study of the Brain Circulation by Rapid Serial Angiography of the Carotid Artery. Acta. Radiol., Suppl., 140, 1-119.
220. Guttman, L. 1936. Physiologie und Pathologie der Liquormechanik und Liquordynamik (Physiology and Pathology of the Mechanics and Dynamics of the Cerebrospinal Fluid). Handbuch der Neurol., 7, 2, 135-180.

221. Hale, A. R. and Reed, A. F. 1963. Studies in Cerebral Circulation Methods for the Qualitative Study of Human Cerebral Blood Vessels. Amer. Heart. J., 66, 2, 242-266.
222. Hardy, J. D. 1964. IN: Physiological Acceleration Problems in Space Exploration. Springfield, 152-195.
223. Henry, J. P., Gauer, O. H., Kety, S. S. and Kramer, P. 1951. Factors Maintaining Cerebral Circulation During Gravitational Stress. J. Clin. Invest., 30, 3, 292-299.
224. Hershgold, E. J. and Steiner, S. H. 1960. Cardiovascular Changes During Acceleration Stress in Dogs. J. App. Physiol., 15, 6, 1065-1068.
225. Hill, L. 1896. The Physiology and Pathology of the Cerebral Circulation, an Experimental Research. London.
226. Himwich, W. A., Knapp, F. M., Wenglarz, R. A., Martin, J. D. and Clark, M. E. 1965. The Circle of Willis as Simulated by an Engineering Model. Arch. Neurol., 13, 2, 164-173.
227. Hodes, P. T., Campoy, F., Riggs, H. E. and Bly, P. 1953. Cerebral Angiography Fundamentals in Anatomy and Physiology. Amer. J. Roentgenol., 70, 1, 61, 62.
228. Holzer, W., Polzer, K. and Marko, A. 1945. Rheokardiographie (Ein verfahren der Kreislaufforschung und Kreislaufdiagnostik) (Rheocardiography (A Method of Circulation Research and Diagnosis)). Vienna.
229. Howard, P. and Glaister, P. H. 1964. The Effects of Positive Acceleration Upon Cerebral Blood Flow. J. Physiol., 172, 39p, 40p.
230. Hürthle, K. 1927. Blutkreislauf in Gehirn (Circulation of the Blood in the Brain). Handbuch d. norm. u. pathol. Physiol., 10, 1-29.
231. Ingvar, D. and Lassen, N. 1965. Methods for Cerebral Blood Flow Measurements in Man. Brit. J. Anaesth., 37, 4, 216-224.
232. Isikava, H. 1959. A Metrological Study of the Blood Capillary Density of the Rhoinbencephalon, Spinal Cord and the Peripheral Nerves in the Cat. Fukuoka igaky zassi. Fukouka acta. med., 52, 11, 4275-4292.
233. Jacob, P. 1900. Klinische und experimentelle Erfahrungen über die Duralinfusion (Clinical and Experimental Results Concerning Dural Infusion) Dtsch. med. Wschr., 3, 46-48.
234. Jacobi, W. 1923. Bestehen den Unterschiede im Eiweissgehalt des Liquor Cerebrospinalis in Verschiedenen Höhen (The Existence of Differences of Albumin Content of the Cerebrospinal Fluid at Different Altitudes). Münch. med. Wschr., 70, 870-872.
235. Jacobson, I., Harper, A. M. and McDowall, D. G. 1963. Relationship Between Venous Pressure and Cortical Blood Flow. Nature, 200, 4902, 173-175.
236. Jacquet, M. 1950. Piezographie, electro-phonocardiographie combinees et exploration analitique de l'etat regional des arteres (Combined Piezography and Electrophonocardiography, an Analytical Examination of the Regional Condition of Arteries). Arch. mal. coeur, 43, 3, 247-264.
237. Jenkner, F. L. 1962. Rheo-encephalography. Springfield.
238. Kanai, H. 1965. The Accuracy of Pulsatile Blood Flow Pattern Measured by an Implantable Electromagnetic Flowmeter. IN: Digest of 6th Intr. Conf. on Med. Electr. and Biol. Engng., Tokyo, 46-47.
239. Katz, L. N. and Kolin, A. 1938. Carotid Blood Flow with Electromagnetic Flowmeter. Amer. J. Physiol., 122, 3, 788-804.
240. Keller, Ch. T. 1930. Untersuchungen über die Gehirndurchblutung. I. Mitteilung: Gibt es eine Autonomie der Gehirngefässe (Investigations

Concerning Cerebral Blood Circulation. Communication No. 1. Is there an Autonomy of the Blood Vessels of the Brain?) Arch. exper. Pathol. u. Pharmacol., 154, 357-380.
241. Keller, Ch. T. 1939. Die Regelung der Blutversorgung des Gehirns (Regulation of the Blood Supply to the Brain). Z. ges. Neurol. u. Psychiat., 167, 281-300.
242. Kety, S. S. 1948. The Blood Flow, Vascular Resistance and Oxygen Consumption of the Brain in Essential Hypertension. J. Clin. Invest., 27, 511-518.
243. Kety, S. S. and Schmidt, C. F. 1945. Cerebral Blood Flow in Man. Amer. J. Physiol., 143, 53-66.
244. Kinnen, E. 1965. Impedance Plethysmograph. IN: Digest of 6th Int. Conf. on Med. Electr. and Biol. Engng., Tokyo. 66-67.
245. Knoll, Ph. 1886. Über die Druckschwankungen in der Cerebrospinalflussigkeit und den Wechsel in der Blutfulle der centralen Nervensystems (Variations of Pressure in the Cerebrospinal Fluid and the Change of Blood Volume of the Central Nervous System). Sitzungsber. Kais. Akad. Wissensch., 93 1/5, 217-248.
246. Koepcken, H. P. 1962. Concepts of Servo-control and Rhythmicity in the Theory of Cardiovascular Regulation. IN: Proc XXIInd Int. Congr. Physiol., Sci., 1, Part I, Leyden, 44-52.
247. Lamb, L. E. 1964. An Assessment of the Circulatory Problem of Weightlessness in Prolonged Space Flight. Aerospace Med., 35, 5, 419-420.
248. Lamb, L. E., Iohnson, R. N., Stevens, M. and Welch, B. E. 1964. Cardiovascular Deconditioning from Space-Cabin Simulator Confinement. Aerospace Med., 35, 5, 420-428.
249. Landahl, H. D. 1958. On the Estimation of Cerebral Blood Flow Obtained From Electroplethysmographic Observations. Bull. math., biophys., 20, 2, 161-167.
250. Lassen, N. 1959. Cerebral Blood Flow and Oxygen Consumption in Man. Physiol. Rev., 39, 2, 183-238.
251. --- 1964. Autoregulation of Cerebral Blood Flow. Circulat. Res., 15, Suppl. 1-201-1-204.
252. Lassen, N. and Munck, O. 1955. The Cerebral Blood Flow in Man Determined by the use of Radioactive Krypton. Acta. Physiol. Scand., 33, 1, 30-49.
253. Lassen, N. and Ingvar, D. H. 1961. The Blood Flow of the Cerebral Cortex Determined by Radioactive Krypton. Experimentia (Basel.), 17, 42, 43.
254. Lassen, N., Hoedt-Rasmussen, K.,Sörensen, S. C., Shinhoy, E., Cronquists, S., Bodforss, B. and Ingvar, D. H. 1963. Regional Cerebral Blood Flow in Man Determined by Krypton. Neurology, 13, 9, 719-727.
255. Legait, E. 1947. Bourrelets valvulaires et bourrelets sphincteriens au niveau des arteres cerebrales chez les vertebres (Valvular and Spincteral Thickenings in the Cerebral Arteries of Vertebrates). Arch. Biol. (Liege), 58, 4, 447.
256. Levine, M. 1930. Electrical Skin Resistance During Hypnosis. Arch. Neurol. and Psychiat., 24, 5, 937-943.
257. Leyden, E. 1886. Beiträge und Untersuchungen zur Physiologie und Pathologie des Gehirn (Contributions and Experiments Relating to the Physiology and Pathology of the Brain). Pflüg. Arch., 35, 519-559.
258. Liebman, F. M., Pearl, J. and Bagnos, S. 1962. The Electrical Conduction Property of Blood in Motion. Phys. in Med. and Biol., 7, 2, 177-193.

259. Lindberg, E. F., Sutterer, W. F., Marshall, H. W., Headley, R. N. and Wood, E. H. 1960. Measurement of Cardiac Output During Headward Acceleration Using the Dye-Dilution Technique. Aerospace Med., 31, 10, 817-834.
260. Ludwigs, N. 1954. Über ein Modifikation der Methode nach Gibbs zur lokalisierten Durchblutungmessung des Hirngewebes und die Gültigkeit der damit erhoben Befunde. (A Modification of Gibbs' Method of Measuring Local Blood Circulation of the Brain Tissue and the Validity of the Findings thus Obtained). Pflüg. Arch., 259, 35-42.
261. Ludwigs, N. and Schneider, M. 1954. Über den Enfluss des Halsympathikus auf die Gehirndurchblutung (The Effect of the Cervical Sympathicus on Brain Circulation). Pflüg. Arch., 259, 43-55.
262. Mangold, R. 1954. Stoffwechsel und Kreislauf des menschlichen Gehirns "Übersicht." (Metabolism and Circulation of the Human Brain. "Survey"). Schweiz med. Wschr., 84, 237-243.
263. Mann, H. 1937. Study of Peripheral Circulation by Means of an Alternating Current Bridge. Proc. Soc. Exptl. Biol. and Med., 36, 5, 670-673.
264. Marotta, S. F. 1962. Circulatory Responses of Anaesthetized Dogs to Elevated Intra-Pulmonary and Intraabdominal Pressures. Aerospace Med., 33, 5, 557-570.
265. Mayerson, H. S. 1940. The Influence of Posture on Blood Flow in the Dog. Amer. J. Physiol., 129, 2, 421-422.
266. Mays, K. 1882. Über die Bewegungen des menschlichen Gehirns (Motions of the Human Brain). Virch. Arch., 88, 125-164.
267. McDonald, D. A. and Potter, J. M. 1951. The Distribution of Blood to the Brain. J. Physiol. and Pathol., 114, 356-371.
268. McQueen, J. D. and Ieanes, L. D. 1962. Influence of Hypothermia on Intracranial Hypertension. J. Neurosurg., 19, 4, 277-288.
269. Meyer, I. S. and Hunter, J. 1957. Polarographic Study of Cortical Blood Flow in Man. J. Neurosurg., 15, 282-399.
270. Meyer, I. S. and Gotoh, F. 1961. Interaction of Cerebral Hemodynamics and Metabolism. Neurology, 11, 4, 46-65.
271. Miller, P. B., Johnson, R. L. and Lamb, L. E. 1964. Effects of Four Weeks of Absolute Bedrest on Circulatory Functions in Man. Aerospace Med., 35, 12, 1197-1200.
272. Miyakawa, K. 1965. Blood Pressure Oscillation Caused by Automatic Control of Blood Supply to the Brain. IN: Digest of the 6th Int. Conf. on Med. Electr. and Biol. Engng. Tokyo. 42-43.
273. Mosso, A. 1881. Über Kreislauf des Blutes im menschlichen Gehirn (Blood Circulation in the Human Brain). Leipzig.
274. Murray, K. D. 1964. Dimensions of the Circle of Willis and Dynamic Studies Using Electrical Analogy. J. Neurosurg., 21, 26-28.
275. Myerson, A. and Loman, J. 1932. Internal Jugular Venous Pressure in Men. Arch. Neurol. and Psychiat., 27, 4-6, 836-940.
276. Noordergraaf, A., Verdouw, P. D. and Boom, H. B. 1963. The Use of an Analog Computer in a Circulation Model. Proc. Cardiovasc. Diseases, 5, 5, 419-439.
277. Nyboer, J. 1960. Electrical Impedance Plethysmography. Springfield.
278. O'Connel, J. E. A. 1943. Vascular Factor in Intracranial Pressure and Maintenance of the Cerebrospinal Fluid Circulation. Brain. 66, 3, 204-228.

279. Pedrazzini, F. 1938. De la circulation cerobrospinale, particulierement par rapport de la force centrifuge sur la systeme et sur la circulation generale chez les aviateurs. (Cerebrospinal Circulation, Especially with Reference to Centrifugal Force on the System and on the General Circulation in Aviators). Presse med., 60, 1104-1107.
280. Polzer, K., Schuhfried, F. and Heeger, H. 1960. Rheography. Brit. Heart J., 22, 1, 140-148.
281. Porye, J. G. 1946. Studies of the Arterial Pulse Wave, Particulary in the Sorts. Acta Physiol. Scand., 42, suppl. 13, 1-68.
282. Pratesi, F., Nuti, A. and Sciagra, A. 1957. Reografia cranica (Cranial Rheography). Minerva Medica, 48, 7, 3223-3229.
283. Quinke, H. 1872. Zur Physiologie der Cerebrospinal Flussigkeit (Physiology of the Cerebrospinal Fluid). Arch. Anat. u. Physiol., Leipzig, 153-177.
284. Ranson, S. W. and Clark, S. L. 1935. The Anatomy of the Nervous System. Philadelphia and London.
285. Read, R. C., Kuida, H., Hiroshi and Johnson, Y. A. 1957. Effect of Alterations in Vasomotor Tone on Pressure Flow Relationship in the Totally Perfused Dog. Circulat. Res. 5, 6, 676-682.
286. Rapela, C. E., Green, H. D. 1964. Autoregulation of Cerebral Blood Flow. Circulat. Res., 15, 2, Suppl. 1-205-1-211.
287. Regelsberge, H. 1930. Tagesrhytmik and Reaktionstypen des Polarisationswider (Diurnal Rhythm and Reaction Types of Polarization Resist (in complete). Z. ges. exptl. Med., 70, 3/4, 438-440.
288. Rein, N. 1928. Die Thermo-Stromuhr (The Thermocurrent Chronometer). Z. Biol., 87, 5, 393-418.
289. Reinmuth, O. M., Scheinberg, P. and Bourne, B. 1965. Total Cerebral Blood Flow and Metabolism. Arch. Neurol., 12, 1, 49-67.
290. Richt, H. 1846. IN: Rukovodstvo po khirurgicheskoy anatomii (Handbook on Surgical Anatomy). St. Petersburg, 1885.
291. Richter, C. 1929. Physiological Factors Involved in the Electrical Resistance of the Skin. Amer. J. Physiol., 88, 596-616.
292. Riser, M. 1936. La Circulation Cerebrale. (Cerebral Circulation). Rev. Neurol., 65, 1060-1173.
293. Rosenblum, W. I., Zweifach, B. W. 1963. Cerebral Microcirculation in the Mouse Brain. Arch. Neurol., 9, 4, 414-423.
294. Rosomoff, H. L. and Zugibe, F. T. 1963. Distribution Intracranial Contents in Experimental Edema. Arch. Neurol., 9, 1, 26-34.
295. Rossanigo, F. and Meineri, G. 1961. Comportamento di alcune grandezze respiratorie in soggetti sottoposti ad accelerazioni secondo diversi assi corporei (Characteristics of Certain Respiratory Measurements in Subjects Exposed to Accelerations Along Various Axes of the Body). Riv. med. aeronant. spaz., 24, 4, 485-500.
296. Rushmer, R. F., Beckman, E. L. and Lee, D. 1947. Protection of the Cerebral Circulation by Cerebrospinal Fluid Under the Influence of Radial Acceleration. Amer. J. Physiol., 151, 2, 355-365.
297. Ryder, H. W. 1952. Effect of Changes in Systemic Venous Pressure on Cerebrospinal Fluid Pressure. Arch. Neurol. and Psychiat., 68, 2, 175-179.
298. Ryder, H. W. and Espey, F. F. 1952. Influence of Changes in Cerebral Blood Flow on the Cerebrospinal Fluid Pressure. Arch. Neurol. and Psychiat., 68, 2, 165-169.

299. Ryder, H. W., Espey, F. F., Kimbel, F. D., Penka, E. L. Rosenauer, A., Podolsky, B. and Evans, J. P. 1952. Modification of Effect of Cerebral Blood Flow on Cerebrospinal Fluid Pressure by Variations in Craniospinal Blood Volume. Arch. Neurol. and Psychiat., 68, 2, 170-174.
300. Ryder, H. W., Espey, F. F., Kimbell, F. D., Penka, E. J., Rosenauer, A., Podolsky, B. and Evans, J. P. 1953. Mechanism of the Change in Cerebrospinal Fluid Pressure Following an Induced Change in Volume of the Fluid Space. J. Lab. Clin. Med., 41, 428-435.
301. Ryder, H. W., Espey, F. F., Kristoff, F. V. and Evans, I. P. 1951. Observation on the Interrelationships of Intracranial Pressure and Cerebral Blood Flow. J. Neurosurg., 3, 1, 46-58.
302. Sachs, E., Wilkins, H. and Sams, F. S. 1930. Studies on Cerebrospinal Circulation by New Methods. Arch. Neurol. and Psychiat., 23, 1, 130-152.
303. Salathe, A. 1876. Recherches sur le mechanism de la circulation dans la cavitée cephalorachidienne (Investigations Concerning the Mechanism of Circulation in the Cerebrospinal Cavity). Travaux du lab. de Marey, 11, 345-401.
304. Scheinberg, P. 1958. A Critical Review of Circulatory Physiology as it Applies to Cerebral Vascular Disease. Ann. Int. Med., 48, 5, 1001-1016.
305. Scheinberg, P. and Stead, E. A. 1949. Cerebral Blood Flow in Male Subject as Measured by the Nitrous Oxide Technique. Normal Values for Blood Flow, Oxygen Utilization, Glucose Utilization and Peripheral Resistance with Observations on the Effect of Titling and Anxiety. J. Clin. Invest., 28, 1163-1171.
306. Schneider, M. and Schneider, D. 1934. Untersuchung über die Regulierung der Gehirndurchblutung (Research on the Regulation of Cerebral Circulation. I. Mitteilung (Communication I). Arch. Exper. Pathol. u. Pharmacol., 175, 606-639.
307. Schroeder, H. A. 1953. Hypertensive Diseases, Causes and Control. Philadelphia.
308. Schwan, H. 1956. Electrical Properties of Body Tissues and Impedance Plethysmography. IN: Simp. of Volume Registration, New York. 31-46.
309. Seipel, J. H., Liemnowicz, S. A. R. and O'Doherty, P. S. 1964. Cranial Impedance Plethysmography-Rheoencephalography as a Method of Detection of Cerebrovascular Disease. IN: Cerebral Ischemia, Springfield, 162-180.
310. Shanker, R. 1963. Cardiovascular Responses to Head-Stand Posture. J. Appl. Physiol., 16, 5, 987-990.
311. Shenkin, H. A. and Novac, P. 1954. Clinical Implications of Recent Studies on Cerebral Circulation of Man. Arch. Neurol. and Psychiat., 71, 2, 148-159.
312. Shenkin, H. A. and P. Novac. 1961. The Control of the Cerebral Circulation. J. Amer. Med. Assoc., 178, 4, 390-393.
313. Sicutery, F., Ricci, H. and Romangnoly, E. 1959. L'onda pulsative del liquido cefalo-rachidiano studiato con metod electromanometrico (Pulse Wave of the Cerebrospinal Fluid Examined by the Electromanometric Method). Min. Med., 50, 18, 637-641.
314. Sieven, V. O. 1897. Experimentall Untersuchungen über den Einfluss der Korperstellung und Respiration auf die Gehirnbewegungen bei Hunde (Experimental Investigations on the Effect of Posture and Respiration Upon Brain Motions in Dogs). Biologie, 34, 504-548.

315. Sigmann, E., Koiln, A., Katz, L. N. and Jochim, K. 1937. Effect of Motion on the Electrical Conductivity of the Blood. Amer. J. Physiol., 118, 708-719.
316. Sigwart, H. 1954. Zur Frage der intracraniallen Hirnpulsation (The Question of Intracranial Brain Pulsation). Deutsch. J. Chir., 278, 115-132.
317. Simonson, E. 1964. Cerebral ischemia: Introduction. In: Cerebral ischemia. Springfield, XI-XVIII.
318. Sokoloff, L., Landau, W. M. Freygang, W. H., Rowland, L. P. and Kety, S. S. 1955. Normal Values for Regional Blood Flow in Cat's Brain. Fed. Proc., 15, 132.
319. Solomon, H. C., Thompson, L. J. and Pfeiffer, H. M. 1922. Circulation of Phenolsulphonpthalein in the Cerebrospinal System. J. Amer. Med. Assoc., 79, 13, 1014-1020.
320. Spiegel, E. and Wohl, M. 1935. The Viscerogalvanic Reaction. Arch. Int. Med., 56, 2, 327-341.
321. Strand, M. 1965. Modern Physiology. The Chemical and Structural Basis of Function. London-New York.
322. Strecker, H. 1922. Experimenteller Beitrag zur Frage des Liquorzirkulation beim Menschen (Experimental Contribution Concerning the Question of Cerebrospinal Fluid Circulation in Man). Münch. Med. Wschr., 69, 50, 1726-1738.
323. Sugar, O. 1961. Discussion of Use and Limitations of Angiography. Neurology, 11, 4, Pt. 2, 91-97.
324. Suzuki, H. and Motokawa, K. 1965. Heated Thermistor Method of Measuring Local Blood Flow in the Brain. IN: Digest of the 6th Int. Conf. on Med. Electr. and Biol. Engng., Tokyo, 62.
325. Symon, L., Tshikawa, S. and Meyer, J. 1963. Cerebral Arterial Pressure and Development of Leptomeningeal Collateral Circulation. Neurology, 13, 3, 237-250.
326. Thompson, S. 1961. A Radioisotope Method for Studying Cerebral Circulation. Arch. Neurol., 5, 6, 580-590.
327. Thurow, K. and Kramer, K. 1959. Die Reaktionsweise der glatten Muskulatur der Nierengefässe auf Dehnungreize und ihre Bedeutung fur die Autoregulation des Nierenkreislaufes (The Character of the Reaction of Smooth Muscle of the Vessels of the Kidney to Stretching Stimuli, and the Significance for Autoregulation of Circulation in the Kidney). Pflüg. Arch., 268, 3, 188-203.
328. Dela Torre, E., Netsky, M. and Meschan, J. 1959. Intracranial and Extracranial Circulations in the Dog: Anatomic and Angiographic Studies. Amer. J. Anat., 105, 343-362.
329. Watson, J. P., Cherniack, N. S. and Zechman, F. W. 1960. Respiratory Mechanics During Forward Acceleration. J. Clin. Invest., 39, 11, 1737-1743.
330. Walter, F. K. 1910. Studien über den Liquor Cerebrospinalis (Studies on the Cerebrospinal Fluid). Monatschr., Psychiat., 28, 80-147.
331. Weeks, A. and Alexander, L. 1939. The Distribution of Electrical Current on the Animal Body. An Experimental Investigation of 60-cycle Alternating Current. J. Indust. Hyg. and Toxicol., 21, 16, 517-526.
332. Weinman, J. and Ben-Yaakov. 1965. The Physical and Physiological Basis of Photoplethysmograph. IN: Digest of the 6th Int. Conf. on Med. Electr. and Biol. Engng., Tokyo. 54-59.

333. Weise, H., Schild, W. and Siemons, K. 1955. Über die Beziehungen der Liquordynamik zum Blutkreislauf (The Relationships Between Dynamics of the Cerebrospinal Fluid and Circulation of the Blood). Z. ges. inn. Med., 10, 17, 829-831.
334. Wever, R. and Ashoff, J. 1956. Durchflussmessung mit der Diathermostromuhr bei pulsierender Stromung (Flow-Through Measurement With the Diathermocurrent Chronometer in Pulsed Flow). Pflüg. Arch., 262, 2, 152-168.
335. Wiggers, C. J. 1954. Circulatory Dynamics. New York.
336. Witterer, E. 1937. Eine neue Methode zur Registrierung der Bluströmungsgeschwindigkeit am uneröffneten Gefäss (A New Method of Recording the Rate of Blood Flow in the Intact Vessel). Z. Biol., 98, 26-36.
337. Wolff, H. G. 1936. The Cerebral Circulation. Physiol. Rev., 16, 545-596.
338. Wolff, H. S., McCall, J. and Baker, J. A. 1962. Semiconductor Electrometer Amplifiers. Brit. Commun. Electron., 9, 120-122.
339. Wood, E., Lingberg, E. F., Code, C. F. and Baldes, E. J. 1963. Effect of Partial Immersion in Water of Response of Healthy Men to Headward Acceleration. J. Appl. Physiol., 18, 6, 1171-1185.
340. Wood, E., Nolan, A. C., Donald, D. E. and Cronin, L. 1963. Influence of Acceleration on Pulmonary Physiology. Fed. Proc., 22, 1024-1034.
341. Woolsey, C. 1915. Experimental Subarachnoid Injections of Trypan Blue. J. Nerv. Ment. Dis., 42, 477-481.
342. Wrawne, M. K. and Fidzsimons, J. T. 1959. Electrocardiographic Changes During Positive Acceleration. Brit. Heart J., 21, 1, 23-30.
343. Wyatt, D. 1961. Problems in the Measurement of Blood Flow by Magnetic Induction. Phys. in Med. and Biol., 5, 3, 289-320.
344. Wyburn, C. M. 1960. The Nervous System. New York-London.

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